



Key Issues Dialogue: Hemophilia

Featuring thought leaders in the hemophilia community

CSL Behring produces safe, high-quality plasma-derived biotherapies for the treatment of hemophilia and other rare and serious diseases. Nanofiltration, pictured here in CSL Behring's state-of-the-art facility in Bern Switzerland, physically removes viruses in plasma.



Key Issues Dialogue: Hemophilia

Featuring Dr. Gabriele Calizzani, Chris James, Brian O'Mahony, Thomas Sannié, Dr. Uwe Schlenkrich, Alain Weill, Dr. Lutz Bonacker, Luis A. Cruz, Rüdiger Gatermann, Dr. Albrecht Gröner, Dennis Jackman, Dr. Mathias Jürs, and Dr. Stefan Schulte.

European hemophilia and CSL Behring representatives examine access to care and other issues impacting the hemophilia community at CSL Behring, Marburg, Germany

CSL Behring representatives recently met with leaders of European hemophilia societies in Marburg, Germany for a discussion of the state of hemophilia care. Marburg is the location of CSL Behring's largest production plant, with 20 product lines focused on plasma proteins. Participants spent two days visiting the Marburg site and a plasma center in Offenbach. In Marburg they heard presentations from CSL Behring experts and engaged in an open discussion of issues concerning the hemophilia community, particularly in Europe.

CSL Behring representatives also discussed the company's initiatives in quality, safety, research, innovation and corporate responsibility. CSL Behring is committed to producing high-quality, safe and effective biotherapies to improve the quality of life for people with rare and serious medical conditions worldwide.

This *Dialogue* includes a panel discussion among conference participants and summaries of four individual presentations in Marburg. Much was learned and we are pleased to share it with you.

Research and Development

RÜDIGER GATERMANN: *We'd like to open this discussion by examining the current state of research and development for bleeding disorders. Are there research ideas that as a community you think we should be looking at?*

BRIAN O'MAHONY: I appreciate your commitment to the rarer products, like the fibrins and concentrates, the Factor X, Factor XIII. There is very little choice in these situations. There is a very small number of patients with congenital fibrinogen deficiency, but up to now they have been treated primarily with Cryoprecipitate, which has safety issues.



I believe we need data for the results of prophylaxis in adults. More and more adults change from on-demand therapy to prophylaxis. So far the insurance companies have approved. But we will likely see a cut in public spending in the next few years...

UWE SCHLENKRICH

CHRIS JAMES: One of the key things for us as a patient group is choice. I think it is good to see other products perhaps coming onto the market. In certain areas, Factor VIIa and Factor IX, there are restrictions in terms of patient choice.

RÜDIGER: *It is often said that the research that is done for rare disease might eventually also be beneficial for more common diseases. Would you agree with this statement?*

STEFAN SCHULTE: Yes. What I normally like to do is to look at the phenotype of these rare diseases and then get an idea where the factor could also be used. From this you can consider other clinical indications.

MATHIAS JÜRS: I can refer to an example that also deals with the C1 esterase inhibitor. When you look at systemic inflammatory response syndrome, you might observe a general edema similar to the edema seen in patients suffering from hereditary angioedema who lack C1 esterase inhibitor. There have been investigations showing that the C1 esterase inhibitor is working quite well in these patients. This shows where there may be expanded indications for the product in acquired conditions.

LUTZ BONACKER: Part of our commitment is providing information in an open, transparent and factual manner to make sure that you have what you need in order to do your work. Is there anything else that you feel we should be focusing on?

UWE SCHLENKRICH: Perhaps what we are doing in Germany would be of interest. We created an overview of products licensed in Germany. Every two years we ask the manufacturers of these products to provide us with information in response to specific questions such as, where is the plasma from and how do they inactivate it? As a result, we have more information about how many units are in a vial and a number of other issues. We collect this data and then publish it for patients so they can see the differences between the products that are available.

RÜDIGER: *What else needs to be done in the field of data collection?*

UWE: I believe we need data for the results of prophylaxis in adults. More and more adults change from on-demand therapy to prophylaxis. So far the insurance companies have approved. But we will likely see a cut in public spending in the next few years and it is important to be able to provide data that shows this therapy is more effective for patients—but it cannot be more expensive.

BRIAN: On that point, over the last several months we completed a survey with the hemophilia societies in the UK, France, Sweden and Ireland. We gathered data on 58 young adults with hemophilia between the ages of 20 and 35. We looked at their treatment regime and quality of life, including the number of bleeds per annum and the time missed from work, school or college. In Sweden, these young men have been on prophylaxis since they were two years of age and continue right into adulthood.



Many also do not understand rare diseases such as primary immune deficiency and that there is a much higher cost to manufacture therapies to treat these diseases.

DENNIS JACKMAN

In Ireland, UK and France, the vast majority of the young men started off with on-demand therapy. Some are now on prophylaxis, some are on-demand.

When we look at the results, they are quite striking. The average number of bleeds per annum in Sweden was about three per annum, compared to about 15 in the other countries. The average time missed from school, work, or college in Sweden was half-a-day per year. In France, UK, and Ireland, it varied from 5 to 15 days per year.

On a relatively small data sample, it clearly shows that young adults with hemophilia who have always had prophylaxis have a far superior quality of life.

LUTZ: If you start prophylaxis at a later stage in life, you have a positive impact on athroopathy. I think that is one way to approach it. We also need to show how treatment impacts quality of life. That is why we are doing the HyQuoL study of ultimately 120 patients. We need to take a look at transitional life events. For instance, when many teen-patients move out of home or go to university, they don't stay on the treatment. We want to help them understand how their life is impacted.

DENNIS JACKMAN: *How about payment? Is that a concern of the community?*

CHRIS: There is no substitute for direct conversation with those who control the purse-strings and make budget decisions. We have to be "in the room" when these discussions take place.

BRIAN: Again, it comes back to data. I think patient organizations are in a position to gather data very quickly. When taking a survey at a conference, don't make it too onerous. The key is to pick the right questions and data can be gathered quickly.

What we have to do is protect the relative position of hemophilia. At the moment, hemophilia is the only condition that I am aware of where the healthcare system will pay a very large amount of money on an annual basis to provide patients with a good quality of life. If you look at the annual cost of prophylaxis for a child, it would exceed the cost of a liver transplant or open-heart surgery. And yet it is funded year after year. We have to ensure the current payment policy for prophylaxis isn't changed or diminished.

DENNIS: One of the challenges is education. Many government people do not truly understand what hemophilia is versus all the other conditions. Many also do not understand rare diseases such as primary immune deficiency and that there is a much higher cost to manufacture therapies to treat these diseases.

CHRIS: It isn't just a budget issue. The decision-making process is not always responsive. We have to educate governments and health administrations about making ethical decisions regarding high-cost treatments.



It (reference networks) works well, but there is still room for improvement. Some centers still don't have video capability or a social worker attached to the center.

ALAIN WEILL

Treatment Centers

LUTZ: *How do we achieve consensus on what the treatment objectives are? I think it's important to have a goal in mind in terms of where the process should lead.*

MATHIAS: It's important to identify the populations at risk. I think that is where the current discussion is really going. People are starting to understand that the on-demand treatment for adults suffering from hemophilia is not always the best treatment. There is certainly a group of adult patients who need prophylaxis for their entire life. As for governments, they will only pay for patients at risk. So we need to provide data identifying these groups.

UWE: It calls for continuous surveillance of their physicians and cooperation with treatment centers.

RÜDIGER: *That would be a task of treatment centers or expert centers. Are these treatment centers prepared to serve hemophilia patients at the high level of care that is established in Europe? Or is there room for improvement? For some, it may be a matter of maintaining the high standards that we have already, and for others it might be setting up of the first expert center for rare disease. Where are the gaps?*

BRIAN: There is always room for improvement. But if you look at certain rare diseases, there are some countries where there are no treatment centers for those diseases. For many very rare conditions, it is practical to set up a national reference center for that condition. For hemophilia, you have the well-established model of comprehensive care centers. So, a country might have 1, 5 or 25, depending on the size of the country. I think the need for reference centers for hemophilia is less obvious than for other rare conditions, because the comprehensive care model is well accepted. In relation to a need for improvement, if you look at the European Union, the European Community, the Factor VIII per capita usage varies from 8.4 in Sweden to 0.4 in Romania. That is a twenty-three-fold difference in the same community. Clearly, there is room for improvement.

DENNIS: Reference networks could play a role in this regard. Technology can be leveraged in bringing much needed information and services to those countries.

BRIAN: France is one country that put that in place. They have a rare disease action plan and designated reference centers for hemophilia and von Willebrand disease.

ALAIN WEILL: Yes, and it works well, but there is still room for improvement. For instance, some centers still don't have video capability or a social worker attached to the center.

THOMAS SANNIÉ: Rarely, but it occurs, doctors view it as a very good opportunity to be a director or member of a center of expertise for hemophilia because it provides



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THOMAS SANNIÉ

opportunities to publish and travel across the world. Unfortunately, as a result of these opportunities they may not spend enough time with their patients. And they also may not know how to justify their budget and position inside the hospital.

UWE: We have the same problem in Germany. Doctors go out and establish their own small centers and everybody is very keen to have the “world’s most comprehensive care center” associated with his or her name, even if it has only five patients.

DENNIS: There was discussion about European reference centers having standards that go along with being called a reference center. In other words, to be a reference center requires certain capabilities, metrics, and outcomes. Maybe that could help the situation you just described.

UWE: Yes, but it is not so easy to convince other physicians that they have to fulfill these criteria.

DENNIS: *Are the centers ordered to meet criteria?*

UWE: In Germany the medical board of the German Hemophilia Society has fixed criteria for the quality of a center and judges which center fits in which criteria.

CHRIS: In the UK there is a triennial audit to meet the requirements of being a comprehensive care center.

BRIAN: In Ireland it is the same situation.

LUTZ: It might be interesting to look at benchmarks in obstetrics, gynecology and oncology similar to the breast centers where it is necessary to have both a certain number of procedures and meet defined quality criteria.

CHRIS: We find one of the problems is that patients don’t actually know what to expect. They have never read the National Service Specification for hemophilia care. They have no idea of the services to which they should get access and how often. We just produced a very simple leaflet for patients to make them more aware of the services they should be provided.

DENNIS: So quality control in the centers is from the top down but the consumer has a role too.

CHRIS: When you survey the hemophilia population in the UK about their treatment and care, about 85% of people say their hemophilia treatment care is excellent. But actually they have nothing to compare it to. What we are trying to achieve is some consistency of treatment.

SUMMARY PRESENTATION BY CSL BEHRING

COMMITMENT TO COAGULATION**Mathias Jürs**, Commercial Operations Central Europe

The discussion on inhibitors is a long-standing one. Multiple plasma-derived products have been compared with single plasma-derived and single recombinant products with regard to inhibitor risk. In the review published by White and Paisley from Sheffield, there seems to be a higher risk on inhibitor generation when it comes to multiple plasma-derived products instead of single plasma-derived products, which was reported to be even less compared to single recombinant products. What we have learned from this and other publications is that there seems to be multiple inhibitor-triggering factors; one of those may be product-associated.

If there is a difference in inhibitor risk between recombinant and plasma-derived factor VIII concentrates, what could cause this difference? One candidate is von Willebrand factor, others are discussed.

Research shows that when hemophilic mice are administered von Willebrand factor, plasma-derived Factor VIII, recombinant VIII and recombinant VIII with a plasmatic preparation of von Willebrand factor, the recombinant factor VIII doesn't seem to react that positively. This derives from laboratory data; there is no clinical study yet.

The discussion on inhibitors in hemophilia patients receiving Factor VIII concentrates, either plasma-derived or recombinant Factor VIII products, is not conclusive yet. Our company monitors the discussion. And we have several research projects in Central Europe, where we support investigators.

Where will this all lead? The answer may be found in a publication from Kurnik and others—*New Early Prophylaxis Regimen in Hemophilia*—in *Hemophilia 2010*. The publication reports an interesting finding. When very small amounts of Factor VIII are administered at a young age, e.g.—250 IU of Factor VIII per week for eight weeks—there is no bleeding, surgery or other manipulation and the dosage is increased according to the clinical presentation, there seem to be fewer inhibitors compared to starting with a very high dose and a rigid prophylactic regime. We're very interested in the further exploration of this point.



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MATHIAS JÜRS

SUMMARY PRESENTATION BY CSL BEHRING

COMMITMENT TO COAGULATION**Lutz Bonacker**, Commercial Development

CSL Behring is committed to coagulation. In addition to our focus on safety and the future product pipeline, we constantly think about the current use of our products. We offer one of the broadest ranges of products for congenital coagulation factor deficiencies including Factors I, II, VII, VIII, IX, X and von Willebrand factor. Furthermore we are introducing these products both in new countries and in new indications.

We have a very broad offering of Factor VIII products, both plasma derived and recombinant, and we are continuously working on improving them. We have one of the few Factor Xs that are available. It is actually a very small product, but it is something that we as a company are committed to providing to the patients who value it. As for Factor XIII, we have been providing it to patients in the US for almost a decade.

We are committed to making things as easy as possible for patients. We can not fulfill the wish for an oral Factor VIII or an oral Factor IX, but we are working on extending the half-life of these coagulation factors which will lead to less frequent infusions. We are also working on smaller initiatives such as ease of handling administration and reconstitution of the factor concentrate. For instance in the reconstitution device we developed technology which ensures that the water jet is directed towards the wall so that the cake dissolves more easily. Furthermore it includes a conical spike, so that there is less risk of losing vacuum when product is reconstituted.

We continually examine data, not just in the registrational trials but also once the product has been launched. This is done through our internal monitoring system and also in collaboration with international databases.

Last but not least, we are sponsoring the HyQuoL study which is observing quality of life in patients who are being treated with recombinant Factor VIII therapy and are at an age where transitional life events such as moving away from home for college occur. This will help to better understand the needs of teenagers with hemophilia.



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LUTZ BONACKER



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BRIAN O'MAHONY

National Rare Disease Plans

DENNIS: *We've mentioned here that countries will be developing national rare disease plans. Is this something that the community is looking at?*

BRIAN: We need to be aware of any moves within our countries to develop rare disease action plans and to see how that best fits in with the optimum model of hemophilia care. We need to be in the room when those decisions are being made, and not hit with a plan that is completed afterwards.

RÜDIGER: *In Europe, the Europlan is in charge of examining the national plan papers and implementation strategies to ensure they match the intent of the national plan. Maybe Europlan will take up the task of benchmarking the proposals that are coming up from member states. Some countries have hemophilia councils, which include hemophilia societies, medical experts and governmental representatives. Would that be also a model to expand across Europe?*

BRIAN: I think it is an excellent model, but I am biased on this. We have a national hemophilia council, which is the official statutory body that makes recommendations and advises the Minister and health authorities on all aspects of hemophilia care and treatment. They come to us with decisions on which hospital should get additional resources or consultants. We audit the treatment centers and we look at the development of care on a national basis. The only other country in Europe where there is a statutory body such as this is Georgia.

I am convinced that you need, whether it is statutory or non-statutory, a formal body. You need a body where the Ministry of Health and the paying authority are joined in the room by the clinicians and by the hemophilia patient organization. You are there as part of the decision making process.

ALAIN WEILL: *Who would represent industry in these bodies?*

UWE: In Germany we have a roundtable once every year, and we invite the representatives of every company which provides clotting factors in Germany. At this table are the physicians, our medical board and the German hemophilia society. So far, we haven't invited politicians. At this table we discuss every problem we see. The historical background was safety issues, and now we are getting more into other problems, like the centers and criteria for the centers. We had, I would say, good experiences with these roundtables.

CHRIS: In the UK we have had a hemophilia alliance for many years. It is a multidisciplinary group with health professionals and patient groups. As part of that, there has always been an industry forum. I think going forward we need to focus that

industry forum on particular outcomes—things industry would like to see in terms of the UK as a whole. It is important that the industry has a voice in this and perhaps we can project that voice through our hemophilia alliance.

DENNIS: So in the development of national plans we are talking about how hemophilia specifically is trying to make sure there is some statutory guidance on the process.

BRIAN: Or on general issues that would affect all of industry at the same time. I come back to what is sort of Advocacy 101. We always say to societies: “If you are going to the Ministry of Health and you cannot get the doctors and the patient organizations to agree on what you submit beforehand, you are in trouble.” I would say the same thing to industry.

Safety Issues

DENNIS: *Are there other concerns the community has that we should talk about? Yesterday there were many questions at the plasma center.*

BRIAN: One current issue is donor deferral—men having sex with men (MSM) donor deferral, for example in the case in Canada. There is a lot of pressure to eliminate the lifetime deferral of MSM donors based on what is seen as discrimination as opposed to science or the precautionary principle. There is a broader debate going on about plasma underpinning the whole issue of voluntary remunerated versus non-remunerated donors and the source of plasma. In Europe you can’t use UK or Irish plasma at the moment. We are importing plasma from the US because of the lower risk of variant CJD. But, how will that change if the FDA in the United States decides to change the donor deferral for MSM donors? Would that not be a major concern?

ALBRECHT GRÖNER: I would say for the known blood-borne viruses—HIV, HBV, HCV—it would not significantly affect safety. Because of the measures in place by every manufacturer, an infection in the donor would be detected by donation screening using serological and nucleic acid amplification technique/polymerase chain reaction (NAT/PCR) methods. And we know from our research that our virus inactivation methods are able to deal with a very high virus load from these three known viruses. Before HIV and especially HCV was known and could be tested for, pasteurization and S/D treatment resulted in virus inactivation. We need to be vigilant to new or emerging viruses and we need to have robust virus reduction steps in place.

BRIAN: *You stated earlier that the whole point here is to minimize the amount of window period donations going into the pool. Doesn’t what you just said contradict that?*



I think going forward we need to focus that industry forum on particular outcomes—things industry would like to see in terms of the UK as a whole.

CHRIS JAMES

SUMMARY PRESENTATION BY CSL BEHRING

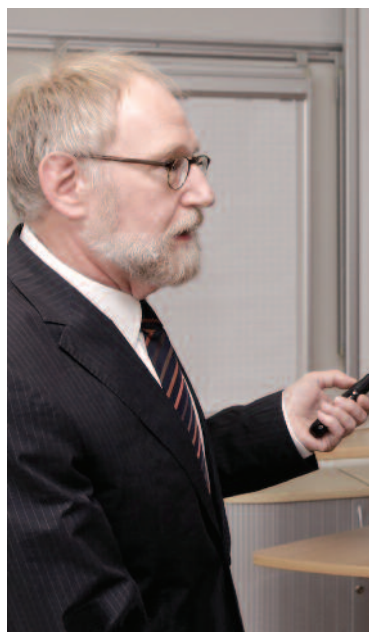
QUALITY AND SAFETY
(CSL Behring Integrated Safety System)

Albrecht Gröner, Virology

I'm pleased to discuss pathogen safety issues including our approach to producing safe and efficacious pathogen-free products. It's no secret that recipients of blood transfusions and plasma-derived products were infected in the past by blood-borne viruses, especially human immunodeficiency virus (HIV), hepatitis C virus (HCV) and hepatitis B virus (HBV). However, today all plasma-protein manufacturers have effective virus inactivation and removal steps implemented in the manufacturing process. As a result there is no longer a measurable risk of infection by HIV, HBV and HCV. Pasteurized coagulation factor concentrates, now more than 25 years on the market, are without any proven virus transmission. The same is true for the solvent/detergent (S/D) treated products for enveloped viruses, but not for non-enveloped viruses.

In addition to these standard virus inactivation processes, we have implemented other measures in the manufacturing process to increase the pathogen safety margin. These include donor selection, donation as well as fractionation pool testing, and release of these compounds if non-reactive.

The safety of the starting material for plasma-derived products is very high; a fact that is documented in the plasma master file, which is a European document. It is based on the selection of donation centers and donors, and on the testing of donations for blood-borne viruses. Only donations which are non-reactive for viral markers and virus genomic material are released for further processing. Our starting material has minimal, if any, virus load of blood-borne viruses, and the manufacturing virus inactivation-removal processes have been demonstrated to clear known and currently emerging blood-borne pathogens.



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ALBRECHT GRÖNER



Nobody has a right to give blood. Everybody has a right to offer to give blood, but nobody has a right to give blood if safety is questionable.

BRIAN O'MAHONY

ALBRECHT: No, not really, because testing would be required at each donation of every donor. In the case of plasmapheresis donations, we would have the inventory hold in place. If the donor would seroconvert or be NAT/PCR reactive, an infection would be discovered and the donations in inventory hold—which tested non-reactive but which may be below the detection limit of the assays—would be discarded.

It looks slightly different for whole blood donations and recovered plasma because the inventory hold is not possible. The distance between donations is so long that when the subsequent donation is reactive, we don't know if the first donation was just below detection limit of the NAT assay or was really from a non-infected donor. In general, I believe collecting plasma from risk groups would not result in a considerable increase in virus load for the known viruses that are tested for. The issue is different for viruses that are really unknown to be transmissible by blood transfusion and/or not tested for. We know that there is a potential increased risk in MSM individuals to transmit further viruses, as sexually transmitted diseases are rising in the MSM population. Therefore, the potential risk will be, in my opinion, too big to accept such donors.

UWE: *How would you handle it if the FDA lifted the ban?*

DENNIS: We realize that the community is very concerned about the lifting of this ban. At the same time, the gay community is very upset about this as well. Our position, and it has become the position of the industry, is that it should be a science-based decision. If there is data that still indicate that there is a higher risk due to MSM, then the ban should remain in place. If the data does not support that, then it is open to question.

BRIAN: It is not so much this issue in itself but what it portends. It is a fact that the industry has made the products as safe and effective as they could over the last 25 years. Here you have almost a sense of déjà vu with the early 1980s, where you have governments and regulating authorities coming around and changing safety measures or not implementing safety measures because of political pressure. Blood donation by definition is discriminatory. Nobody has a right to give blood. Everybody has a right to offer to give blood, but nobody has a right to give blood if safety is questionable. That applies to plasma as well of course.

The Future of R&D and Gene Therapy

DENNIS: *Clearly one big concern in our discussion is maintaining the layers of safety. What about R&D? Is there any big research question you want to have answered? Looking ahead 15-20 years, what do you think will be the next big innovation?*

SUMMARY PRESENTATION BY CSL BEHRING



We have a very broad plasma product portfolio, including basically all the coagulation factors needed for treatment of hemophilia. We draw on this expertise to develop new products that improve patients' quality of life.

STEFAN SCHULTE

RESEARCH AND INNOVATION (Plasma-derived and recombinant therapies)

Stefan Schulte, Research and Development

Our goal is to maintain an innovative state-of-the-art research and development (R&D) program using the latest technology and fulfilling all the regulatory requirements with regard to safety.

Another important aspect of R&D at CSL Behring is our clear focus on protein-based therapy. Our Marburg operation, for example, is focused on new protein therapies for the treatment of coagulation disease. We have a very broad plasma product portfolio, including basically all the coagulation factors needed for treatment of hemophilia. We draw on this expertise to develop new products that improve patients' quality of life. This includes identifying new clinical indications which can be treated with the factors we derive from plasma. Our expertise in coagulation led us to explore other applications for our coagulation factors including controlling bleeding during cardiac surgery and organ transplantation. We are now close to the end of a phase II study using Factor I in aortic surgery and as a replacement for fresh frozen plasma, Cryo and other blood products.

Currently we are also working on recombinant coagulation factors. Our goal is to develop coagulation factors for the next generation. Our focus is the half-life extension of coagulation factors so that they work longer in the recipient. For CSL Behring, albumin is a very good choice to try to accomplish half-life extensions by albumin infusion technology. This involves fusing coagulation factor with a short half-life with albumin which has a fairly long half-life. Using genetic methods both are made recombinant. We have completed the pre-clinical target validation and we have an exclusive license from Novozymes for the whole albumin fusion technology and also for other coagulation factors. Furthermore we are very optimistic that we can begin clinical trials for Factor IX soon.

Other research priorities include longer half-life products, development of products that are less immunogenic, inhibitors, getting patients to come forward for clinical trials, and the principles for conducting trials.



I think progress has been made. Now we need convincing proof of concept in a real congenital disease.

STEFAN SCHULTE

STEFAN: Inhalable Factor VIII. Or maybe someone will advance gene therapy to the point where it can be used to cure a disease.

DENNIS: *Are we even part of the way there?*

STEFAN: I think progress has been made. Now we need convincing proof of concept in a real congenital disease. When researchers have a convincing case, they might enter the hemophilia community at some point. I do not think they will go directly into the hemophilia community because the risk is too high.

DENNIS: There is talk that there could be a combination: gene therapy and replacement therapy.

STEFAN: I think the big advantage of gene therapy is that it has a chance to cure the disease.

DENNIS: *On that very forward-looking note, are there any other comments or questions before we close?*

ALAIN: *What are the basic reasons for a company like yours deciding to integrate the blood or plasma bank into your organization and not have a separate system—and buy plasma or blood from an independent body?*

DENNIS: It is a number of things. It is quality, control, and safety, because we are controlling those units from the beginning all the way through. It is also assuredness of supply. We want to make sure that we have that because it is so essential. Plasma is the lifeblood of what we do. Our patients rely on it. We rely on it.

BRIAN: I would like to come back to a previous point—about looking 20 years into the future. I can look back to 1990 when we developed an early strategic plan with WFH, called the decade plan. It was a very ambitious plan. One of the actions was not gene therapy or a cure; it was delivery of a cure. It was recognized that even if you had gene therapy, if it was so expensive that it was out of the reach of the vast majority of people with hemophilia around the world, the demand for it would be limited. We are in the situation where we are all living in countries where we have excellent therapy available to us. It is safe; it is efficacious. We can also look forward to further developments, in longer-acting, longer-half-life factors, making treatment even more effective and less frequent.

So, in a sense, gene therapy as a cure for us is not as imperative as it is for people in India, China, Africa, and Latin America. But, the key issue there is if gene therapy becomes available as a cure, I think you would have a situation where you would have a different pricing structure for developing and emerging countries. It would be terribly sad to see those of us in the Western world able to get gene therapy and a cure—or our grandchildren and children, and those in developing and emerging countries not being able to access that.



We now have a better understanding of some of the key issues and concerns with which your patient-members deal every day. A dialogue shouldn't stop; it shouldn't be one day.

DENNIS JACKMAN

DENNIS: That is an important point.

BRIAN: Because if we had a cure available for the wealthier countries, then industry, by definition, the manufacturers of Factor concentrates would wind down their activities. So, you might actually start to see a worse situation for people in developing countries. Would that be the case if they didn't have access to the cure?

DENNIS: We then still would have therapies going to that part of the world. Obviously, we are interested in providing support and access through WFH. I would hope that we would still be engaged in trying to help them deliver care. But the biggest challenge in the rest of the world is access to the care.

BRIAN: Let's all keep in mind that the biggest safety risk is bleeding to death.

RÜDIGER: *Brian's comment brings us full circle back to where we began our dialogue about the state of hemophilia care and current issues concerning the hemophilia community. Dennis, do you have a closing perspective that you care to share?*

DENNIS: Yes, thank you Rüdiger. I think we learned a good deal from our dialogue. From CSL Behring's standpoint, we now have a better understanding of some of the key issues and concerns with which your patient-members deal every day. A dialogue shouldn't stop; it shouldn't be one day. Let us continue this dialogue in the future. Thank you for participating in the dialogue and for your important contribution toward raising awareness of the challenges that impact the hemophilia community.



About the Participants

Dr. Gabriele Calizzani

President, Italian Hemophilia Society

Gabrielle Calizzani is a severe hemophilia A patient. He has been actively involved in the Italian Hemophilia Society since he was a teenager and is currently the society's president and a member of the European Hemophilia Consortium Steering Committee. He specializes in hygiene and preventive medicine and has been a consultant of different Italian institutions.

Chris James

Chief Executive, Hemophilia Society, United Kingdom

Chris James is responsible for the strategic and operational management of the Society to ensure that it meets its overall aims and objectives, and maintains its standing as an influential patient organization which advocates on behalf of people with bleeding disorders. He has spent more than 20 years working for voluntary sector organizations in the UK. He is a member of the Department of Health and Hemophilia Alliance Advisory Group and a number of other national bodies for bleeding disorders and rare and long-term health conditions. He has a particular interest in long-term medical conditions and the provision of support services.

Brian O'Mahony

Chief Executive, Irish Hemophilia Society

Brian O'Mahony represents the Irish Hemophilia Society (IHS) on the statutory National Hemophilia Council and as vice chairman of the Tender Commission established by the Irish Government. He previously served as chairman of the IHS and as president of the World Federation of Hemophilia (WFH). He continues to volunteer with WFH, EHC and national member organizations. His activities include writing, advocating and facilitating trainings on strategic planning, national procurement systems and advocacy and lobbying. Brian O'Mahony has severe Hemophilia B.

Thomas Sannié

Member, Board of Directors, French Hemophilia Association

As President of the Chapter of region Ile de France in charge of public health and education, Thomas Sannié is a member of the board of the French Hemophilia Association.

Dr. Uwe Schlenkrich

Member, Board of Directors, German Hemophilia Society

Uwe Schlenkrich is also a member of the Steering Committee of the European

Hemophilia Consortium (EHC). He has studied medicine with a specialization in medical microbiology and epidemiology. For over 15 years he has been a member of the Arbeitskreis Blut (Working Group Blood), an advisory group of the German Ministry of Health.

Alain Weill

Member, Board of Directors, French Hemophilia Society

Alain Weill is the father of a young hemophiliac A severe. He joined the French Hemophilia Society in 2006 after having spent 34 years holding various positions in the air transport industry. As a member of the society's board of directors he is in charge of European and International Affairs.

Dr. Lutz Bonacker

Vice President, Global Commercial Development, CSL Behring

Lutz Bonacker has broad expertise in a range of therapeutic areas and has worked a number of years as head of the global coagulation group within Commercial Development at CSL Behring.

About the Participants

Luis A. Cruz

General Manager, Spain and Portugal, CSL Behring

Luis A. Cruz is a pharmacist by training and has more than 25 years of experience in the pharmaceutical business. He joined CSL Behring in 1996 as marketing director for Spain. He has worked in global coagulation marketing and as regional marketing director for Western Europe. He is currently based in Barcelona and serves as general manager for the Iberian team.

Rüdiger Gatermann

Director, Public Affairs—Europe, CSL Behring

Rüdiger Gatermann is responsible for development and execution of public affairs and policy strategies in Europe. Mr. Gatermann has held positions in public affairs and external relations in the pharmaceutical industry since 1987. He has a master's degree in administrative science from the University of Konstanz, Germany.

Dr. Albrecht Gröner

Director, Preclinical Research & Development—Pathogen Safety, CSL Behring

Albrecht Gröner has more than 35 years experience in virology. He oversees virus and prion validation studies in Marburg and performs risk assessments of

pathogen transmission by plasma-derived and biotechnological products.

Dennis Jackman

Senior Vice President, Public Affairs, CSL Behring

Dennis Jackman is responsible for optimizing stakeholder impact on CSL Behring's ability to provide lifesaving therapies worldwide. Previously he served as executive director of the Plasma Protein Therapeutics Association for North America, the industry group for advocacy, quality standards and communications. He has held senior public affairs positions in the pharmaceutical and biotechnology industries since 1989.

Dr. Mathias Jürs

Senior Manager Medical Affairs, Commercial Operations—Central Europe, CSL Behring

Mathias Jürs is a specialist in surgery with an interest in hemostaseology, critical care and immunology. He joined CSL Behring in 1998 and has worked in Clinical R&D, the Critical Care Business Unit and in Medical Marketing Central Europe, where he is currently focusing on hemophilia.

Dr. Stefan Schulte

Vice President, Research & Development Marburg, CSL Behring, Marburg

Stefan Schulte is responsible for managing the local R&D activities and

leads new product developments from human plasma and recombinant technologies in the field of coagulation and hemophilia in Marburg. He has 15 years of experience in the pharmaceutical industry and held various technical and international management positions in research, process development and validation.

About CSL Behring

CSL Behring is a leader in the plasma protein therapeutics industry. Committed to improving the quality of life for people with rare and serious diseases, the company manufactures and markets a range of plasma-derived and recombinant therapies worldwide.

CSL Behring therapies are indicated for the treatment of coagulation disorders including hemophilia and von Willebrand disease, primary immune deficiencies, hereditary angioedema and inherited respiratory disease. The company's products are also used in cardiac surgery, organ transplantation, burn treatment and to prevent hemolytic diseases in newborns.

CSL Behring operates one of the world's largest plasma collection networks, CSL Plasma. CSL Behring is a subsidiary of CSL Limited, a biopharmaceutical company headquartered in Melbourne, Australia. For more information, visit www.cslbehring.com.



CSL Behring is a leader in the research and development of biotherapies for the treatment of rare and serious conditions. At its facility in Marburg, Germany, pictured here, CSL Behring produces coagulation, wound-healing and specialty products.

