EHC Newsletter

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Editor: Amanda Bok
Editorial Committee: Jo Eerens, Radoslaw Kaczmarek, Brian O'Mahony, Olivia Romero-Lux, Laura Savini
AISBL EHC registered office: Rue du Marché aux Herbes 105 b14, 1000 Brussels, Belgium
Tel. +32-2 521 11 50, Fax +32-2-520 68 66, Email office@ehc.eu
No. 887.106.966

President and CEO Report

Longer-acting haemophilia therapies

We are at the beginning of a very exciting time for the treatment of haemophilia. At the recent Conference of the World Federation of Hemophilia (WFH) there were updates on the progress with the development of longer-acting factor concentrates (see the article of Giuseppe Mazza on pg 36). Several companies are making steady progress in their clinical trials with these new and novel products using three distinct and separate broad methods to modify the FVIII or FIX protein to allow for a longer duration of effective factor levels in the blood. The first longer-acting FIX product called Alprolix was licenced in the United States (US) in March by Biogen and the first longer-acting FVIII product called Eloctate was licenced in June also by Biogen. Further longer-acting products will be licenced in the coming months and years.

Brian O'Mahony, EHC President and Amanda Bok, EHC CEO

In Europe, there will be a delay in the licensing of the new longer-acting products due to the requirements of the Clinical Trial Guidelines of the European Medicine Agency.

These European guidelines mandate that clinical trials in previously treated children must be completed prior to licencing of the products for use in adults whereas in the US and other countries outside the EU, products can be licenced for use in adults once the clinical trial of the products in previously treated children has commenced. The motivation of the European Medicine Agency (EMA) was to ensure that new products are not used to treat children 'off label' before they are specifically licenced for use in children. The practical result of these guidelines is a two to three year delay in the licencing of these new products in the EU compared to the rest of the world. It is likely that the first longer-acting FVIII product will be licenced in the EU in late 2015 or early 2016 with the first longer-acting FIX being licenced shortly thereafter. It is of course possible that they may be licenced and used in non-EU European countries prior to then, but we believe this to be unlikely given the relatively low factor use per capita in many non-EU countries at present and the possibility of higher cost for the new products.

Indeed, the new products may lead to a re-examination of the utilisation of the current generation of products and a re-evaluation of current treatment regimens and attitudes. With current treatment – with prophylaxis three times a week for FVIII and twice a week for FIX – the relative importance of treatment peaks at those intervals in addition to the trough level of one percent (which has always been the main objective of prophylaxis; to keep factor levels above one percent at all times to prevent spontaneous bleeding episodes) will be re-examined. Longer-acting factors hold out the promise of maintaining a trough level of one percent with less frequent infusions but by definition

this will also result in fewer peaks in factor levels. More frequent peaks in factor levels may be very important in those who are very active (for example with sports).

With both current treatments and the new longer-acting products, the validity of a target trough level of one percent must be questioned. This trough level does not prevent all spontaneous bleeds or offer adequate protection to joints. It will certainly not prevent bleeds in joints which have already suffered substantial damage in the past (target joints) from further bleeding episodes or damage.

There is substantial clinical evidence that a trough level of three percent would offer much better protection to joints and result in a substantially lower annual bleed rate in many people with haemophilia. Individualisation of treatment based on pharmacokinetics, individual bleeding pattern, degree of pre-existing joint damage and activity levels is almost certainly the route to optimum treatment in the future.

The companies who manufacture and market the current generation of recombinant factor concentrates will have to respond imaginatively to offer therapeutic choice when the longer-acting factor concentrates come to the market in Europe. The entire business model may have to change. For countries who currently utilise significant amounts of recombinant factor concentrates, there will be competition from the newer products and a re-examination of treatment protocols and paradigms. For countries who do not currently have access to significant quantities of factor concentrates, the availability of longer-acting factor concentrates may provide an opportunity to benefit from potentially lower costs for the current generations of factor concentrates – both recombinant and plasma-derived. Competition may result in lower prices and greater availability.

This remains predicated on competition from longer-acting factor concentrates, which will not occur in any realistic way if only one longer-acting FVIII and one longer-acting FIX are licenced and granted market exclusivity in Europe under the EU Orphan Medicinal Product Regulation. This would be anti-competitive and result in a monopoly situation leading to less choice, higher costs and a dramatically reduced possibility of greater access to current products for those countries where the need is currently greatest.

EHC have made representations to the the EMA and the European Commission on this vital issue and we also authored a recent editorial in *Haemophilia* on this critical topic (http://onlinelibrary.wiley.com/doi/10.1111/hae.12462/abstract). We are quietly confident that our work will bear fruit and that all the potential new products will be allowed on the market. We look forward to these developments with profound anticipation as we enter an era where the worst sequelae of haemophilia bleeding episodes may be on the verge of being minimised for many people with haemophilia, and previously-unforeseen improvements in quality of life begin to seem possible. We will continue to keep you appraised of developments in this area and we will hold an EHC workshop on New Technologies in haemophilia, which will look at all aspects of development (including clinical, treatment protocols and economics) with the new products later this November.

New hepatitis C therapies

We are also at the beginning of a very exciting time for the treatment of hepatitis C (see articles of Declan Noone on pg 33 and article of Radoslaw Kaczmark on pg 37) as, in fact, the revolution in the treatment of hepatitis C will be even more profound. The specific newsletter of the Irish Haemophilia Society on hepatitis C and HIV issues – *Positive News* – reports in detail on the proceedings from the

European Association for the Study of the Liver conference and is available to download from the EHC website. A veritable abundance of new therapies for hepatitis C are under development and several are already licenced in Europe.

These new therapies offer the realistic hope of a cure for all with hepatitis C. The current triple therapy regimes have been successful in approximately 75-80% of people with haemophilia. Nonetheless, a significant number have failed with these therapies and the course of treatment is long with many side effects. The majority of people with haemophilia treated have to undergo 48 weeks of treatment. The new therapies offer a 90-100% cure rate with a treatment regime of 12-24 weeks with a very significant reduction in side effects. There are many new drugs available and becoming available in different combinations capable of treating even the most clinically difficult-to-treat-patients – those who are pre liver transplant or post-transplant or those with advanced cirrhosis. HIV co-infection does not appear to be a barrier to success with these new treatments. The therapeutic future looks very promising for people with haemophilia who still live with chronic hepatitis C infection or HIV and hepatitis C co-infection.

While clinical developments look very promising, the main obstacle our community may face will be economic. These new treatments will be expensive. We will have to work and advocate nationally and at a European level to optimise the availability of these new therapies for people with haemophilia throughout Europe.

Advocacy video to promote haemophilia recommendations

The EHC released its first advocacy video outlining each of the seven final recommendations for haemophilia treatment and care that came out of the Kreuth III initiative earlier this year (see pg 12). These recommendations are the result of the third Wildbad Kreuth consensus meeting on 'Optimal use of clotting factors and immunoglobulins,' which took place from 26-27 April 2013 in Germany following two previous consensus meetings in 1999 and 2009 on blood safety and optimal clinical use of blood components. This third edition was organised by the Paul-Ehrlich-Institut, the University of Munich and the European Directorate for Quality of Medicine and Healthcare (EDQM), part of the Council of Europe. More than 100 experts from 36 national authorities participated in the 2013 consensus meeting. The resulting final recommendations issued by these experts were published in *Haemophilia* this spring (http://onlinelibrary.wiley.com/doi/10.1111/hae.12440/abstract). They offer an updated appraisal of the state-of-the-art optimal clinical use of clotting factors and are widely regarded as the new international reference. These recommendations are reasonable, achievable and form a roadmap for maintaining and where necessary improving haemophilia care and treatment in all European countries. The EHC advocacy video is available here on its YouTube channel (https://www.youtube.com/watch?v=XxWAw40W4Ms) and we strongly encourage its widespread use and dissemination. The EHC will also feature a live, interactive and inter-generational debate on three of these recommendations during a symposium in its upcoming Conference in Belfast, Northern Ireland, from 3-5 October. The objective of this debate will be to stimulate thinking about the implementation of these recommendations, prepare our community for potential obstacles and counter-arguments, and bring all generations into this important conversation.

Youth Leadership Workshop

The EHC's first youth leadership workshop was successfully held in Amsterdam, the Netherlands, from 4-6 July (see pg 18). It brought together 15 young and highly dedicated volunteers who actively participated in the interactive workshop about volunteerism, engagement, effective dialogue between generations and successful project/team management. A productive and constructive first conversation was born in this workshop, which will hopefully continue in the months and years to come – the EHC will certainly do its part to keep it going!

Round Table on 'von Willebrand Disease'

The EHC held a Round Table of Stakeholders on current clinical issues in von Willebrand Factor and Disease (VWD) in Brussels on 16 June. Hosted by Prof Paul Giangrande, Chairman of the EHC Medical Advisory Group (MAG), the Round Table brought together eminent medical speakers and more than 40 participants – many of whom were patients with VWD – to discuss definitions, diagnosis, prophylaxis, choice of products, the role of von Willebrand Factor in inhibitors and personal experiences with the disorder. A rich and stimulating discussion followed the presentations. The event is captured faithfully by Dan Farthing from Haemophilia Scotland on pg 15. This was the first EHC Round Table dedicated exclusively to VWD and builds on a Round Table in 2011 on 'Women and bleeding disoders.'

EHC News

25 Years of EHC: A perspective from physician

By Laura Savini, EHC Communication and Public Policy Officer

To celebrate its 25th anniversary the European Haemophilia Consortium (EHC) is running a series of articles looking back at the evolution of the haemophilia community in Europe and looking at present and future challenges. For the second edition of the EHC 2014 newsletters, Laura Savini speaks to four physicians who, through their professional experiences, have an intimate knowledge of the community and have been able to witness the changes that occurred in the past 25 years. Prof Paul Giangrande (Oxford University Hospitals), Prof Wolfgang Schramm (Rudolf Marx Foundation), Prof Erik Berntorp (Lund University) and Prof Jerzy Windyga (Warsaw University) have given their personal accounts on how the haemophilia community has been reshaped and what the current challenges are that face patients and physicians alike.

In the bleeding disorders community there is, for understandable reasons, a very intimate relationship between the people affected by bleeding disorders and their physicians. For the patient community, physicians have been a partner of choice to support advocacy actions and to liaise with government officials as well as experts to resort to for medical and scientific expertise. Physicians have also been strong supporters of active patient groups and have often helped them to get established and developed. However, these relationships were severely tainted by the HIV and Hepatitis C (HCV) contamination, though now seem to have returned to a positive relationship.

Prof Schramm started his medical career in 1973 with Prof Rudolf Marx at the University of Munich. Prof Marx was the founder of the German Society of Thrombosis as well as the German Society of Haemophilia. This had a great impact on Prof Schramm, who from the very beginning of his work was involved in supporting the emerging patient group. Prof Schramm recalls: “Prof Marx believed that it was the role of physicians to help patients and so with a small group of people he founded the German Haemophilia Society.” As he saw it, in the early stages, patients’ associations were not very well organised and they were reliant on strong physician leaders. In the ensuing years, patients were empowered and developed strong leaders within their own community.

Prof Wolfgang Schramm continues to be active with the EHC

Prof Windyga started his medical career years later in the early 1990s, however he also was immediately involved in patient-physician collaboration. At that time, the Polish Haemophilia Society had a very active President, Mr Zbigniew Sendulka. Prof Windyga describes him as an exceptional person who was very open to collaborate with doctors. Prof Windyga recalls: “Mr Sendulka had a very open personality and could liaise with doctors in a very moderate manner by clearly expressing patients’ needs. These traits made the collaboration with doctors very successful.”

Unfortunately, these good relations were severely tainted during the HIV and HCV contaminations of the 1980s. Prof Berntorp recalls: “When I started my career, the situation in Sweden was not as bad as in other European countries such as France, where both physicians and government representatives were put in jail. Nonetheless patients felt wronged and felt that it was unacceptable that this situation had ever occurred. The HIV contamination catastrophe came as a lighting in a clear

sky, nobody was prepared for it, and with some exceptions it is difficult to personally blame individuals that were mixed in it." This was also the opinion of Prof Schramm who said that this episode caused, understandably, many tensions between patients and physicians and many physicians were disconcerted by the events. Prof Giangrande, who started his career in the early 1980s saw many of this older colleagues go into early retirement because they were shell-shocked by the events and also many physicians were vilified by patient groups. Nonetheless, following this tragedy, some physicians decided to support patients in their legal actions to get compensated for the contamination. Prof Schramm, Prof Giangrande and Prof Berntorp all took an active role in supporting patient groups to obtain compensation for the HIV contamination.

Prof Wolfgang Schramm was the Chair of the German HIV fund, a small group liaising with pharmaceutical companies for compensation of infected patients. The group put heavy pressures on the pharmaceutical industry and it resulted in a compensation fund of 30 million Deutsch Marks.

Prof Giangrande together with other physicians, such as Prof Michael Makris, supported the United Kingdom (UK) Haemophilia Society in getting compensation for the HCV contamination. Prof Giangrande said: "At the time there was not much support from the medical community towards legal actions by the patients' society. In fact, some physicians saw it as accepting part of the responsibility." Nonetheless, Prof Giangrande supported patients' groups both in the UK as well as in Ireland with the Lindsay Enquiry. The support came from providing scientific evidence, something that he and other colleagues did by publishing several articles in major scientific journals. "We published extensively on the epidemiology of HIV and HCV in a series of journals such as the *Lancet*, *Nature* and the *British Medical Journal*."

Prof Berntorp also started his career in the early 1980s and as a young physician he was confronted with the HIV and HCV contamination. He recalls: "When the crisis of the contaminated blood occurred, I was recruited to work on patients with bleeding disorders who had been contaminated with HIV at the centre in Malmö. The position was a delicate one as many of the practising physicians were those who had prescribed the contaminated products. Back then I was seen as the perfect candidate because I was at the beginning of my medical career." He started this work in 1985 at the coagulation department where he was given a package of literature on HIV as background information. With this information in hand, he started a group to map the HIV situation in Sweden for haemophilia patients and their families. "When I started to work with HIV patients to map all HIV transmission in Sweden from factor concentrate, my job was to establish which batch had contaminated which patient. This work allowed me to become an expert on the matter and to support patients during legal trials for compensation. It is something I am particularly proud of," said Prof Berntorp.

Prof Erik Berntorp with a portrait of Ivar Arosenius

Luckily relations between patients and physicians were slowly restored. According to Prof Berntorp, this is partly due to the fact that people understood that the situation was an exceptional one and that nobody had been prepared for it. Also, the advent of better treatments for HIV and cures for HCV helped to appease relations. This is paramount in Prof Schramm's opinion as he believes that patients and physicians need to work together in order to find

the best treatment for each patient. Prof Berntorp also supports this view, although he states that physicians and healthcare professionals remain the experts in their field and have a deeper understanding of the way the medicine works. In his opinion there needs to be some distance to the collaboration and both patients and physicians need to remain independent. Prof Berntorp draws the parallel of physicians not being allowed to treat their own family members. Physicians need to maintain some distance in order to be able to better perform their jobs.

For Prof Giangrande, relations between patients and physicians have overall changed for the better especially following the legacy of HCV and HIV. Haemophilia had been known to be a troublesome medical area and this had deterred some young doctors from into getting in this area, hopefully this will begin to change.

All interviewed physicians supported patient groups not only in their legal actions for compensation of the contamination but also in other areas, including their day-to-day advocacy activities. Prof Giangrande supported the introduction of recombinant products while Prof Berntorp, for instance, supported the implementation of prophylaxis. Prof Berntorp stated that for several years now he has also been involved in some kind of '*crusade*' for implementing prophylaxis especially in North America and he believes he has played an important role in starting prophylaxis in Norway, which began this programme quite late despite the country's good finances.

Prof Paul Giangrande is the Chair of the EHC Medical Advisory Group

Prof Giangrande feels he has been instrumental in implementing the adoption of recombinant product in the UK and other European countries. From early on, Prof Giangrande started to campaign for the introduction of recombinant products and his voice was heard thanks to the prominence he gained during the HIV crisis. "As a young physician, your voice is not immediately heard, you need to work hard and to dedicate a lot to become an expert in the subject matter," said Prof Giangrande. Another advantage that Prof Giangrande had was his fluency in several languages such as Italian, English, French, German and Spanish. "Languages do not only allow to circulate ideas: they also allow you to be culturally sensitive and to better understand issues going on in another culture/ country."

For Prof Windyga, collaboration with patients' groups is a daily business.

"What I have learned in the past 20 years in the clinical practice is that rare diseases are, for obvious reasons, expensive to treat and that for this reason patients with rare diseases struggle to achieve good level treatments. It is paramount to convince politicians that money invested in rare diseases is money well spent," said Prof Jerzy Windyga

Prof Windyga explains: "Healthcare funds should not just be invested in the big medical areas like oncology and cardiology, but they should also be allocated to rare diseases. The general public does not have a good understanding of what is going on. Therefore it is important to continuously work together with patients to reach out to government officials and remind them of this message." In the last 20 years, treatment levels in Poland have gone from just above 0 IU/ capita to 5 IU/ capita, this is

a reflection of the economic progress made by the country. Nonetheless, with the current financial pressure this good level of treatment is threatened and that is why Prof Windyga believes that strong collaboration is necessary now more than ever to ensure that haemophilia and other bleeding disorders can maintain a good level of treatment. In 2007, Poland introduced prophylaxis for patients from 0 to 18 years of age. At the moment, physicians are trying to convince politicians with sound medical evidence that it would be beneficial to extend this regimen to adult patients as well. This is but one of the examples of this daily collaboration between patients and physicians.

One of the first projects developed by Prof Schramm was to advocate for the hiring of a psychologist to support patients who were infected with HIV. At the time, this was not part of the medical services provided to these patients, but he saw the importance of this medical follow-up. Then, in the early 1990s, Prof Schramm started a collaboration with the Austrian Society of Haemophilia. The contact was made because both Prof Schramm and the Austrian Haemophilia Society were working on projects in Romania. Prof Schramm was working to bring clotting factor concentrates to Romania, while the Austrian Haemophilia Society was supporting Romanian patients in developing a patient association. This was the beginning of a long-standing collaboration with both physicians and patients in Romania. Prof Schramm visited the country at least 80 times throughout his career. Prof Schramm was also one of the forces behind the Wildbad Kreuth initiative (see page 12), a series of scientific meetings on the treatment of haemophilia. This initiative was held together with other physicians such as Prof Paul Giangrande and Prof Flora Peyvandi as well as patients' representatives like Mr Brian O'Mahony.

All physicians also invested themselves in ensuring the dissemination of medical training and scientific standardisation. Prof Giangrande was elected Vice-President Medical in 2000 of the World Federation of Hemophilia (WFH) and he remained in this position for two terms. One of his priorities in this position was to improve the quality of the scientific and medical programmes of the WFH Congresses, something he believes has been a success. He also helped to establish the WFH Laboratory Quality Assurance Scheme by persuading the WFH to sponsor this programme.

For the past ten years, Prof Berntorp has also been involved in the Ivar Arosenius[1] Fund, which was established 20 years ago by the Swedish Haemophilia Society for the promotion of research and development in the aid of people with haemophilia. The Fund's Board includes representatives of the medical profession and genetic research as well as representatives of the Swedish Hemophilia Society. In 2012, Prof Berntorp was honoured to give the Arosenius lecture during the WFH Congress that was held in Paris.

"Some ten years ago I started international courses in haemophilia and von Willebrand Disease, first a Malmö University Hospital and then in Asian universities located in Bangkok, Beijing and Kuala Lumpur. The reason we started these courses was to secure expert staff in haemophilia centres for the future. These courses have been extremely successful and attended by over 300 young physicians from all over the world," explained Prof Erik Berntorp.

Prof Windyga also collaborated with the WFH. In 2007, he was asked to coordinate a Twinning project with Moldova. The project lasted for three years and focused on improving laboratory

[1] Ivar Arosenius (October 8, 1878 – January 2, 1909) was a Swedish painter and author of picture books. He was affected by haemophilia and died of complications of the disease.

diagnosis and physiotherapy. The Twinning was so successful that it was recognised in 2009 as '*Twin of the Year*'. At the moment, Prof Windyga has begun a second Twinning project with Albania.

Prof Schramm also held many positions on scientific boards both on patients' associations such as the Medical Advisory Group of the EHC and on scientific bodies such as at the Robert Koch Institut, where he sat on the Blood Working Party. Although, Prof Schramm is not formally affiliated with the EHC any longer, he feels that he has a sense of duty to continue providing scientific and medical advice to the consortium and continues to collaborate with the EHC.

All interviewed physicians agree that the main issue in the haemophilia community remains the lack of availability of treatment worldwide. In Europe in particular, there are still great discrepancies in the level of access to treatment from one country to another. Prof Windyga noted that the most striking disparity is between Western countries located in the European Union (EU) and Eastern non-EU countries. According to Prof Schramm this is certainly due to economic pressure, which cannot be disregarded and this is true not only for traditionally lower income countries like Romania but also for wealthier countries like France, Italy and Sweden. For example, one of the next burning issues in Germany will be the economic appraisal of longer-acting products. In Prof Schramm's opinion, it is part of the duty of physicians to ensure that patients have many different treatment options and this includes advising policy-makers on best treatment options, which should not be solely calculated on economic value.

For Prof Giangrande, another issue is complacency.

"Many people think that we have achieved a lot, but we have real financial threats that already impact how much factor we are able to use. Both doctors and patients should remain vigilant: this is a real problem," warns Prof Paul Giangrande.

For Prof Berntorp, another current problem in the haemophilia community is the lack of diagnosis and the infrastructure to support the diagnosis and delivery of treatment.

Furthermore, the advent of newer generation products also remains a concern. For Prof Windyga the European licensing of longer-acting products is important. In fact, these products reduce the number of injections and this means a significant improvement in the quality of life for patients. For Prof Giangrande, it is important to continue fostering the development of new products and making sure that patients have access to them through clinical trials and European licensing: "At the moment, we are experiencing issues with the Paediatric Investigation Plans (PIP – see article on page 21) and we need to ensure that novel treatment remains affordable." Moreover, for Prof Windyga, gene therapy is the ultimate goal for the cure of haemophilia but this will obviously take some time to realize. Also, caution is needed in term of making sure that it is safe and efficacious for the patient in the long run.

Finally for Prof Berntorp, an issue of great interest is the question of inhibitors. Patients who develop inhibitors are unfortunately in a treatment state that is equivalent to the one in place many decades ago.

In conclusion, the interviewed physicians were very positive about the improvement of patient-physician relationship in Europe. This is also

Prof Jerzy Windyga headed a WFH Twinning between Poland and Moldova

demonstrated by more formal collaborations such as the Memorandum of Understanding (MoU) between the EHC and the European Association for Haemophilia and Allied Disorders (EAHAD). What is certainly true is that physicians strive to work in the best interest of patients through joint advocacy work and maintaining high medical standards. To conclude in the words of Prof Schramm, patients and physicians need to maintain good relations; this is paramount as physicians need to be able to treat patients with the patients consent and not against them. It is essential that physicians see that they are not just treating a condition but that they are in fact treating individuals who, with access to the right treatment, can accomplish anything they wish to.

About Prof Paul Giangrande

Prof Giangrande is consultant haematologist at the Oxford University Hospital's NHS Trust and is Director of the Oxford Haemophilia Centre. He is also the Chair of the EHC Medical Advisory Group. Prof Giangrande completed his training in internal medicine and later specialised in haematology. He studied and worked in the UK, Switzerland and Italy. He was one of the investigators of the first clinical trial for recombinant clotting factors.

About Prof Wolfgang Schramm

Prof Schramm is affiliated with the University of Munich and the Rudolf Marx Foundation. He trained in Internal Medicine with a specialisation in transfusion medicine. For many years, he headed the Department of Haemostasis and the Department of Transfusion Medicine at the Ludwig-Maximilian-University in Munich.

About Prof Erik Berntorp

Prof Berntorp is Professor in Coagulation Medicine disorder at Lund University and Head of Research Unit at the Skåne University Hospital in Malmö, Sweden. Prof Berntorp studied medicine at the University of Lund. He then received his medical training at the Malmö University Hospital, where he specialised in Internal Medicine and Haematology with a focus on bleeding disorders, thrombosis and haemostasis.

About Prof Jerzy Windyga

Prof Windyga is an Associate Professor at the Institute of Haematology and Transfusion Medicine based in Warsaw, Poland. He is also the Head of Department of Disorders of Hemostasis and Internal Medicine and the Director of the Haemophilia Comprehensive Treatment Centre, which is a European reference centre for adults with inherited bleeding disorders in Poland.

Official Launch of the Kreuth III European recommendations for the treatment of haemophilia with coagulation factor concentrates

By Laura Savini, EHC Communication and Public Policy Officer

On the occasion of World Haemophilia Day (WHD), the European Haemophilia Consortium (EHC) held an event at the Paul-Ehrlich-Institut (PEI) in Langen, Germany on 16 April (one day before WHD) to present the 'Kreuth III' European consensus recommendations on the minimum standards for haemophilia care in Europe *(highlighted in the box on the left).*

Kreuth III recommendations

Recommendation 1

In order to optimise the organisation of haemophilia care nationally, it is recommended that a formal body be established in each country to include the relevant clinicians, national haemophilia patient organisation, health ministry, paying authority and (if appropriate) regulatory authorities.

Recommendation 2

The minimum factor VIII consumption level in a country should be 3 International United (IU) per capita.

Recommendation 3

Decisions on whether to adopt a new product should not be based solely on cost.

Recommendation 4

Prophylaxis for children with severe haemophilia is already recognised as the optimum therapy. Ongoing prophylaxis for individual adults should also be provided when required based on clinical decision making by the clinician in consultation with the patients.

Recommendation 5

Children with inhibitors who have failed, or who are not suitable for, immune tolerance therapy (ITI), should be offered prophylaxis with bypassing agents.

Recommendation 6

Single factor concentrates should be used as therapy wherever possible in patients with rare bleeding disorders.

Recommendation 7

Orphan drug designation for a factor concentrate should not be used to hinder the development, licensing and marketing of other products for the same condition, which have demonstrably different protein modification or enhancement.

The recommendations were the result of a two-day scientific meeting held in 2013 in Wildbad Kreuth, Germany, where leading experts from 36 countries came together to define the optimal use of coagulation factor concentrates. The initiative is also known as Kreuth III, because it was the third meeting of this kind. The first meeting took place in 1999. Kreuth III was organised by the PEI, the University of Munich and the European Directorate for the Quality of Medicines and Healthcare (EDQM), an official body of the Council of Europe. Marie-

Emmanuelle Behr-Gross from the EDQM described the Kreuth events as an initiative that creates the conditions of an exemplary cooperation between health authorities, regulators, clinicians, haemophilia patients and the pharmaceutical industry organisations. Prof Wolfgang Schramm (Rudolf-Marx Foundation) a longstanding expert in the haemophilia community and one of the forces behind the Kreuth initiatives, said that in his opinion, the initiative is a successful modus operandi for continuous improvement of haemophilia care and therapies in Europe.

"Although the recommendations cannot be seen as an obligatory document in our country at the moment, they are very important because they remind decision-makers how far we are from the optimum treatment levels and that improvements are necessary," said Tatjana Markovic, Vice-President of the Serbian Haemophilia Society.

The event on 16 April brought together over 40 participants from the patient and medical community as well as regulators and industry. It featured presentations from Kreuth III participants who developed these guidelines. This included leading physicians such as Prof Paul Giangrande, chair of the EHC Medical Advisory Group and Prof Wolfgang Schramm as well as representatives from both agencies supporting the initiative, namely Prof Rainer Seitz (PEI) and Dr Marie-Emmanuelle Behr-Gross (EDQM). Mr Brian O'Mahony, president of the EHC, gave a presentation on the importance and need of such recommendations, claims that were backed up by talks from the President of the Portuguese Haemophilia Society, Mr Miguel Crato and the Vice-President of the Serbian Society, Ms Tatjana Markovic, who through concrete examples in their respective countries demonstrated the need for continuous treatment improvement.

Speakers and EHC staff at the Paul-Ehrlich-Institut

The event led to some fruitful discussions on the next steps for the application of the recommendations. It was noted that in some European countries the level of treatment of haemophilia is still very low and does not come close to the minimum standard of 3 IU/ Capita recommended in the guidelines. Patients' representatives and health professionals need to continuously advocate with national government officials to improve the level of care. It was considered that one way of achieving this minimum level of treatment was to encourage governments to implement measures to bring down costs, such as national tenders. Nonetheless, it was stressed as mentioned in recommendation 3 that the cost of factor concentrates should not be the only criteria when purchasing but that other parameters such as safety, quality and efficacy, also

need to be taken into account. This was further outlined by Prof Paul Giangrande who said, “Product choice must focus on quality and not be compromised by consideration of cost alone. At a time when countries are trying to make savings through national tenders, this is a real and growing concern.” This particular point is a major concern for many European countries at the moment, a fact that Mr Crato reiterated by saying that the quality of medicine should never be a slave of economic circumstances.

Besides the difficulties in accessing products, participants also noted that healthcare institutions are also under continuous pressure to minimise expenditures, which sometimes leads to the assimilation of specialised units into bigger departments. It was noted that in some cases this may in fact jeopardize the expertise of a particular unit. During the meeting, Mr O’Mahony pointed out that this was precisely, why projects such as EUHANET – see pg. 45 - (http://www.euhanet.org/) are so important. By classifying, evaluating and certifying haemophilia treatment centres in Europe, these centres will strengthen their reputation and have a more solid basis on which to claim continuous funding for the services they provide.

Finally, a last point of discussions focussed on an increasing trend amongst patients from lower-income countries in Europe to move to countries that offer better treatment regimens. These host countries are now starting to take note of this phenomenon and there is a concern that they may implement measures to limit patient access to treatment when they relocate within other European countries.

Intervention from Prof Margit Serban on the treatment situation in Romania

The EHC is currently exploring ways to ensure that the recommendations have a strong impact. During the meeting Mr Alain Weill, President of the World Federation of Hemophilia, suggested to seek endorsement from the World Health Organisation, so that these recommendations can benefit not only European patients but all the regions of the world.

Each year, the EHC carries out surveys and it stated its intention to consider surveying the implementation of the seven recommendations in each European country to establish solid factual information about the state of haemophilia treatment in Europe. It has also developed a short video on the recommendations to be used for advocacy by its National Member Organisations. The video can viewed on the EHC YouTube Channel: http://www.youtube.com/watch?v=XxWAw40W4Ms

The Kreuth III recommendations were published in the May edition of the scientific journal *Haemophilia*.

Closing the World Haemophilia Day event Prof Seitz, who kindly hosted the event, said, “We were particularly pleased to host the meeting in the PEI, where patients shared with us their experiences and their views on the impact of the Kreuth recommendations."

EHC Round Table on “von Willebrand Factor and Disease: Current Clinical Issues”

By Dan Farthing, Senior Executive Officer at Haemophilia Scotland

On 16 June 2014, the European Haemophilia Consortium (EHC) held one of its regular Round Table meetings. These events are a fantastic opportunity for healthcare professionals, patients, patient organisations and pharmaceutical companies from across Europe to come together and discuss bleeding disorders. The topic of the meeting was von Willebrand Disease (VWD).

Professor Paul Giangrande opened the event by raising the question on whether it really was appropriate to refer to VWD as a disease. He wondered if a term like ‘deficiency’ or ‘disorder’ might be more appropriate.

Prof Giangrande felt that too often physical explanations for menorrhagia (abnormally heavy bleeding at menstruation) were looked for before a bleeding disorder was considered. He also thought that patient organisations had an important role to play in raising awareness to tackle that problem.

The first presentation highlighted that globally haemophilia is under-diagnosed but that is even truer for VWD. Within Europe there is quite a large range between places like Italy and France, which report quite low levels of VWD, and places like the UK where more people have been diagnosed. During the discussions, this was partly explained by the downsides of being diagnosed, especially if you are not experiencing bleeding problems and live in a country with an insurance-based healthcare system. It might be the case that just by being diagnosed your insurance premiums go up, even if you do not need treatment. In several countries you would only be diagnosed with VWD if you fulfil two of these three criteria:

- Levels of less than 30% von Willebrand Factor (VWF),
- You have bleeding problems,
- You have a family history of VWD.

Pictures from the EHC June Round Table

The most moving part of the meeting was hearing from Ms Baiba Ziemele (President of the Latvian Haemophilia Society). Baiba told us that when she was growing up, Latvia was part of the Union of Soviet Socialist Republics (USSR). Her father knew that he had a bleeding disorder but did not know what it was called or that it could be passed on to his children. Even today she and her family do not know what type of VWD they have and she has been told the laboratory services at the hospital do not have enough qualified personnel to complete the diagnosis project she has been working on with them. She explained how she has taken decisions in her life to reduce her exposure to problems from her bleeding disorder. That choice affects everything from shaving her legs through to her decision not to have children. She spoke about how her sister bravely decided to have a child but that there simply was not the expertise to support her and she had a very difficult experience.

As a patient, Baiba has some simple requests. She wants to know what type of VWD she has, she wants doctors who know more about her condition that she does; and she wants them to be able to help her when she has bleeding problems.

The next presentation was also extremely powerful. Dr Susan Halimeh (Gerinnungszentrum Rhein-Ruhr) gave a presentation about the benefits of prophylaxis treatment for VWD. She highlighted that there were not clear guidelines for how much treatment was suitable for von Willebrand but that the benefits of treatment were impressive. During the discussion on this subject, she and Helen Campbell from the UK, argued that monthly menorrhagia is at least as good a justification for using a prophylaxis treatment regime as getting two or three joint bleeds would be for a man with haemophilia. Women should not be expected to live with menorrhagia when there is a treatment solution. The discussion also recognised that it can be hard but not impossible for clinicians to make the case for the product needed for putting some with VWD on prophylaxis.

Pictures from the EHC June Round Table

Prof Pier Mannuccio Mannucci (Hospital Ca' Granda Foundation) discussed the controversial debate over the use of plasma derived or recombinant products. He acknowledged the important role that von Willebrand Factor (VWF) has in both gastrointestinal (GI) bleeds and menorrhagia. He felt that, where it works, Desmopressin (DDAVP) should be the treatment of choice as it avoids the need for clotting factor and is cost effective. He felt that too often factor products are used when DDAVP could be used. He demonstrated that most of the current plasma-derived factor concentrates contain as much coagulation Factor VIII (FVIII) as VWF. The arrival of new higher concentration products such as Wilfactin or Recombinate will allow clinicians to look at whether FVIII is needed to effectively treat VWD. He told the audience that FVIII often has a long half-life in people with VWD. This means there is a danger of over-treating (peaking) FVIII when people with VWD get a lot of treatment. He thought that this could increase the risk of Deep Vein Thrombosis (DVT) and wondered if the new products

could be used to avoid that. Looking to the future it was his opinion that VWD was not a good candidate condition for gene therapy.

Dr Carmen Escuriola-Ettingshausen's (Hämophilie-Zentrums Rhein Main) presentation turned the meeting to consider the role of VWF in inhibitors. Inhibitors are the biggest current challenge in the treatment of haemophilia. There is an ongoing debate on the vexed question of whether the likelihood of developing an inhibitor is higher with recombinant products than with plasma-derived products. Problems with the studies, which have been carried out so far mean that there is not enough data to make a definitive statement on the issue. Therefore a new study, called SIPPET[2], is currently being carried out. Similarly, there is a lack of validated evidence about whether using products with or without VWF has an effect on inhibitor rates. The experience in Germany - where switching away from a product containing VWF to one without led to a reduction in the success of Immune Tolerance Therapy (ITT) - suggests that VWF might have a role. RESIST[3] is investigating this question. With no firm evidence that one type of product is better than another there is still plenty of work to do.

Pictures from the EHC June Round Table

Staying on the topic of inhibitors we heard from Dr Srini V Kaveri (INSERM, Centre de Recherche des Cordeliers) about the role of immunology in inhibitors. He explained that if your immune system has produced an antigen to FVIII then it was made by your B Cells on instructions from your T Cells after it was presented to them as a potential threat. This means that there are lots of opportunities to use these processes to tackle the question of inhibitor development or to assist with producing tolerance.

Pictures from the EHC June Round Table

The final session was given by Dr Augusto B. Federici (University of Milan) and looked at Acquired von Willebrand Disease (AVWD). In many aspects, progress on VWD is ten to fifteen years behind progress in haemophilia and this is also true for Acquired Haemophilia and AVWD. This is exacerbated by the fact that there is not one single mechanism for AVWD. There is also a need for a good assay (test) when looking for an inhibitor in relation to AVWD. Dr Federici is currently working on setting up an

[2] Survey of Inhibitors in Plasma-Product Exposed Toddlers: http://www.sippet.org/source/home.aspx
[3] Rescue Immune Tolerance Study: http://www.itistudy-resist.com/

Interactive Registry on AVWD, which would be a valuable resource for tackling some of the challenges in this area.

The meeting ended with an extensive discussion. Ms Liz Carroll from the Haemophilia Society (UK) gave an update on their Talking Red awareness raising campaign. Many of the women with VWD at the meeting spoke about their own experiences. Prof Giangrande asked if they had personal preferences on the recombinant vs plasma-derived debate. There were divergent responses ranging from only being comfortable with recombinant to only wanting to be treated with plasma derived.

Helen Campbell from the UK summed it up well by saying that although she shared concerns of many people with haemophilia about plasma-derived products she would take whatever worked best for her. She also stressed that smaller volumes would make a big difference.

Successful youth leadership workshop held in Amsterdam

By Michael van der Linde, Chair of the EHC Youth Working Group

Two years of preparation all came together in the Casa400 hotel in Amsterdam last July, when the first youth leadership workshop hosted by the European Haemophilia Consortium (EHC) was held. After receiving almost thirty applications from active youth volunteers from 20 countries between the ages of 21 and 30, 15 applicants participated in the event. Though 26 was the average age of the participants, the group of youth volunteers was very 'senior,' displaying an intimate understanding of the haemophilia 'world' they are active in. The workshop was deemed a great success, bringing highly motivated young volunteers from the EHC National Members Organisations (NMOs) throughout Europe together to learn and share ideas.

Participants, facilitators and sponsors pose for the group photo

From idea to workshop in two years

One of the groups in action while building their spaghetti tower

The idea of the youth leadership workshop was pitched in 2012 to the EHC Steering Committee and, after finding sponsors for the event in 2013, the project was started and a Youth Working Group was formed. To determine the focus of the workshop an initial needs assessment was held among EHC NMOs, to identify what skills were rated as most valuable for their youth to learn. Following the outcome of the needs assessment, the content of the program was shaped around the topic: 'Turning motivation into action: communicating your ideas into reality.'

Setting the mood for an interactive program

The program consisted of eight sessions spread out over the two days, and relied heavily on contributions and interactions from the youth. Because of the interactive nature of the sessions it was essential to set the mood and make participants feel comfortable with facilitators and each other. Therefore, we started the program on Friday evening with a group building activity; what better way to make people work together than to come up with a frustrating challenge. In a spaghetti-tower-building-challenge, participants had to work in small groups to make the highest possible spaghetti tower while suspending a marshmallow off the ground using only some tape and a small piece of string. After what must have been a very stressful 15 minutes of building time, all groups let their spaghetti structures go with fear and despair clearly showing on their faces. Only one group was able to get their marshmallow off the ground, making them the winners of some delicious Dutch treats.

"All groups let their spaghetti structures go, with fear and despair clearly showing on their faces."

From volunteers to strategic planning, everything you need in a successful project

No project can succeed without volunteers. Therefore, we started the first sessions on Saturday with letting participants think and deliberate about what defines and motivates volunteers, and how you can retain already active volunteers. Supported by presentations from experts in the field and from different perspectives (youth, NMO board and staff), brainstorming sessions were held with participants to get their thoughts going on how they could get more volunteers involved in their projects.

After a well-deserved lunch break, we shifted the focus towards making your project a success. In the first session after lunch on Saturday, titled Internal Communication, we had participants work together in groups, each group tackling a different case-study, deliberating on how they would deal with and communicate during different difficult situations within their NMO. In the Strategic Planning session, participants were once again confronted with different real-life case studies. This time each group did every case study, led by facilitators who accumulated notes and reported back at the end. The case studies of this session were designed to force participants to think of problems from all angles, for example when setting board priorities, a situation which all will most likely see in their own NMOs as well.

Participants brainstorming during one of the real-life case studies

Following a delicious dinner in a Portuguese restaurant on the riverbed of the Amstel and a well-deserved but - thanks to overtime in the FIFA World Cup quarter finals - rather short good nights' rest, we kicked off the Sunday morning with a session on Project Management. After learning the basics of project management, set out clearly by the two facilitators of the session, participants were given a form to fill in their own projects, thus making their initial project plan. After reviewing the project plans during the lunch break, participants were given feedback on their plans, explaining where they could make improvements to be able to deliver a successful project.

Putting all the pieces together

The last session of the workshop consisted of four role plays, done in groups of four. Each participant was given a role, without knowing what the other participants' roles were. The role plays, which were based on real-life scenarios, were designed to let participants see and feel how difficult it can be to get everybody on the same page in meetings, where often people have their own agenda. After a short preparation time, the first four participants confidently took their places at the table and startled every facilitator with their performance. Following a loud applause actors reflected on what had happened during their role play meeting and how the outcome could have been better. The result was a clear improvement on the following role plays, with participants taking into account previous comments, illustrating the high learning curve of the exercise.

One of the participants making his case against the other actors in the role play

Extracurricular festivities

Participants in their shiny new orange outfits on the Saturday evening dinner

Since the workshop was conveniently planned during the heat of the battle of the FIFA World Cup quarter finals and the Dutch were playing against Costa Rica, the Dutch delegates saw no other solution than to dress up everyone in the Dutch national colours and go out to the nearest bar after the Saturday evening dinner to cheer the Dutch football team together. On behalf of the entire Dutch nation, we would like to thank every participant, facilitator and observer for their undivided support during the excruciatingly tense game. No doubt we won the penalty shoot-out because of all of you!

Looking back and looking ahead

Looking back on this first youth leadership workshop as organisers, we think the workshop was a great success. Although organisationally the workshop presented some challenges, having involved more than ten speakers and facilitators, we were pleased to see that participants were able to experience a great weekend. Participants were not only able to learn all aspects of projects-making, but also to get together as youth volunteers and share and exchange ideas. One of the participants illustrated this very clearly in a thank-you message to the organising committee:

"The workshop enabled me to think more strategically in how our NMO should approach youth work. Not only did I learn how to work with project management, but also how good communication and close collaboration with the Board in particular (but also with other stakeholders) could be beneficiary for obtaining the results you want in your projects," said one of the participants.

Looking ahead, I hope that we will be able to set up a consecutive workshop in 2015, opening space for other participants to undergo the same experience, whether it be on the same subject or another.

A word of thanks

I would like to take this opportunity to thank everyone who helped put this workshop together, including the initial youth steering group who drafted the first project proposal (Federico Ruiz Garcia, Lino Hostettler, Steffen Hartwig, Dorothée Fournier de Saint-Jean and Nadège Pradines). I would also like to thank the EHC Youth Working Group, who worked relentlessly to make the workshop a success (Federico Ruiz Garcia as youth representative, Olivia Romero-Lux and Traci Marshall-Dowling from the EHC Steering Committee, Amanda Bok and Laura Savini from the EHC office). Finally, I would like to thank the speakers, facilitators and sponsors (Novo Nordisk, Bayer and Baxter) without whom this workshop would not have been possible.

Günter Auerswald gets appointed to European Medicines Agency Paediatric Committee on behalf of the EHC

Günter Auerswald interviewed by Laura Savini***

Late last year, the European Haemophilia Consortium (EHC) submitted an application to become a member of the EMA Paediatric Committee (PDCO), putting forward Dr Günter Auerswald as the candidate. Dr Auerswald is a former head of the Comprehensive Care Centre for Haemophilia and Thrombosis at the Professor-Hess-Children's Hospital in Bremen, Germany. He retired from this position in 2013 and is currently a Senior Adviser to this Institution. The EHC was delighted to receive confirmation of his appointment last May. The EHC spoke to Dr Auerswald following the decision.

About the PDCO

The EMA PDCO was established by the Paediatric Regulation[4] in 2006 to respond to a public health concern, which was the lack of research and data on the use of medicines in the paediatric population in Europe. This resulted in several problems such as adverse events due to misuse of medicines and wrong dosages.

The Paediatric Regulation created the Paediatric Investigation Plan (PIP) and established the PDCO within the EMA to assess all aspects of medicinal products to treat the paediatric population.

The PIP is a research and development programme aimed at ensuring that the necessary data are generated determining the condition in which a medicinal product may be authorised to treat the paediatric population[5]. In practice, it is a document that sums up the measures that a sponsor will take to demonstrate the quality, efficacy and safety of a particular drug under development for the paediatric population. The PIP immediately became an integral part of the development of medicinal products, irrespective of the targeted population. This means that any sponsor of a novel drug developed for the European market, prior to its marketing authorisation, needs to develop a PIP and to generate data on the use of a particular drug by the paediatric population. In certain cases, the PIP may be waived or deferred if, for example, the treated condition only happens in adults or if the product is likely ineffective or unsafe in the paediatric population. The regulation also specifies that the PIP should not block or delay the marketing authorisation of medicinal products for non-paediatric populations.

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[4] Regulation (EC) No 1901/2006 of the European Parliament and of the Council of 12 December 2006 on medicinal products for paediatric use.

[5] Art. 2(2). Regulation (EC) No 1901/2006 of the European Parliament and of the Council of 12 December 2006 on medicinal products for paediatric use (2006) OJ L 378/1.

The PDCO was established to evaluate PIPs and to assess the validity of the generated data and determine whether the requirement for PIPs could be waived or deferred for a particular drug. It also provides general scientific advice to other EU bodies with regard to paediatric medicinal products and research. The PDCO is composed of representatives from the European Union (EU) Member States, representatives from the EMA Committee for Human Medicinal Products (CHMP) and representatives from patients' organisations and health professionals.

About Dr Günter Auerswald

Dr Auerswald started to work on haemophilia treatment in 1975 until his recent retirement. Throughout his medical career, Dr Auerswald focused not only on haemophilia but also on other bleeding disorders such as von Willebrand Disease and rare bleeding disorders. He also had a particular interest in the prevention of inhibitor formation. On this specific point, he is a believer of the effectiveness of prophylaxis treatment in children, which in his opinion considerably reduces the risk of developing inhibitors as well as joint-damaging and fatal bleeds.

In recent years, Dr Auerswald invested himself in educational projects targeting haemophilia treaters, physiotherapists and nurses from both EU and non-EU countries, an activity that he is currently still involved with. For example, he worked on the PREVENT Project, a series of three-day seminars for health professionals from Europe, the Middle-East and Africa aimed at providing training on how to maximise treatment efficiency with very low amounts of factors concentrates and to reduce inhibitor development.

Dr Günter Auerswald during the EHC World Haemophilia Day event at the Paul-Ehrlich-Institut on 16 April 2014

Dr Auerswald is a member of the German Society of Haemophilia and was for a long time a member of its medical advisory board. He has also been involved in the preparation of national haemophilia plans in countries such as the Ukraine and Russia and has had a longstanding collaboration with Prof Wolfgang Schramm (Rudolf-Marx Stiftung) on projects in Romania.

Dr Auerswald notes that current clinical practices for haemophilia and other bleeding disorders treatment is quite diverse in Europe. For instance, some countries benefit from good levels of treatment that can reach 6 or even 8 International Units per Capita (IU/capita), while other countries like Romania or the Ukraine struggle to supply to its patients even 1 IU/capita. Furthermore, countries with lower treatment are also often quite late in diagnosing and treating inhibitors, which often results in dramatic consequences. Dr Auerswald recalls the tragic story of a Romanian haemophiliac, who developed inhibitors and lost both his legs as a result of severe bleeds that could

not be managed. For him, it is unbelievable that such situations still occur today in Europe. There is still a lot that remains to be done to improve diagnosis and treatment in Europe.

This is especially true for children. In fact, if diagnosed and properly treated at an early age, children with haemophilia and other bleeding disorders can live a normal and fruitful life and avoid joint-damaging or life-threatening bleeds. Dr Auerswald saw these differences first-hand while, for example, carrying out Twinning programmes with the World Federation of Haemophilia in Central American countries such as Costa Rica. There, he was confronted with children as young as ten and already crippled. This was a reality in most of Europe some 30 years ago and since then a huge progress in the quality of treatment was made in Europe. “Treatment is available and there is no reason why people affected by bleeding disorders should be so badly affected by the disease,” specified Dr Auerswald.

There are a lot of opportunities to improve treatment and this should not be prevented by economic barriers. For instance, it is already possible to see significant differences in terms of pricing of factor concentrate units in Europe. Dr Auerswald noted that in the UK, for example, prices are either continuously decreasing or remaining steady thanks to a pricing system based on the Dutch auction model. This allows the government to acquire greater amounts of factor concentrates and to increase the level of care and provide a better quality of life.

Dr Auerswald is conscious of the problems resulting from the off-label use of medicinal products in the paediatric population. In his opinion, there is a great need to collect clinical data for paediatric use and perhaps there should be alternative ways to collect such data than those currently used. In fact, for rare diseases it is often difficult to gather a significant amount of data. Also, there should be further regulatory harmonisation and collaboration between the EMA and the United States’ Food and Drug Administration (FDA) and perhaps PIPs can strengthen this collaboration.

Finally, he felt strongly that children are the future and that we have the knowledge and means to avoid the historic course of the disease if we treat them early. Good results can already be achieved with early prophylaxis and moderate amounts of treatment, which in the long term will bring significant savings to the whole society.

The EHC is delighted to start this formal collaboration with Dr Auerswald and the EHC is confident that his extensive experience both in Europe and in other parts of the world will greatly benefit not only the bleeding disorders’ community but other patients’ groups also.

**Dr Günter Auerswald is a Senior Consultant to the Comprehensive Care Centre for Haemophilia and Thrombosis at the Professor-Hess-Children’s Hospital in Bremen.*

***Laura Savini is the EHC Communication and Public Policy Officer.*

NMO News

First Portuguese parents' conference: The knowledge of today's parents will shape the future of their children.

By Miguel Crato, President of the Board of the APH (Asociação Portuguesa de Hemofilia e de Outras Coagulopatias Congénitas – the Portuguese Haemophilia Society).

April is a special month for all Portuguese people. It was in this month, in 1974, that Portugal took a giant leap towards modernity and knowledge through a democratic revolution.

Forty years later, the Associação Portuguesa de Hemofilia (APH or the Portuguese Haemophilia Association) makes too, a giant leap for awareness and knowledge with its first parents' conference.

APH acknowledges that for parents of children with bleeding disorders, there is a great need for information, training and education on the specificities and challenges of their children's condition.

Indeed, being a parent of a child with haemophilia can be seen, especially in the early days, as a drama, which unfairly happens to a family. The fragility of a child, plus fears about his or her future can bring additional worries and troubles to the family environment.

However, after the initial shock, it is time to face the situation and to find out more about the disease, the right treatment and to join support groups that can help to demystify haemophilia and everything that comes with it.

Participants at the first parents' conference of the Portuguese Haemophilia Society
(Photo courtesy Portuguese Haemophilia Society)

In other words, getting in touch with other parents who have been through similar situations may help not only in fighting potential isolation, but also by improving parents' knowledge of the disease during childhood and adolescence.

Only then can parents get an extensive knowledge of what they need to know, allowing the child to grow in a normal and safe way. Thus, the essential roots that will allow a child and youth to become a conscious and knowledgeable individual are created and this will allow for a perfect transition into adulthood.

On April 4, the beautiful castle town of Palmela, near Lisbon, welcomed forty parents who attended our first conference with great expectations.

The conference was organised in two parts. The first one, called 'Haemophilia and communication' was workshop-based, where we presented parents with three real-life situations.

The first workshop proposed different topics such as: switching treatment for a child without parents' consent; preparing a meeting with the clinician; from a single teacher to several ones and organising the communication about haemophilia in a new school environment; and answering to the letter from a distressed mother whose child was just diagnosed.

All parents actively participated. They were divided into three groups, interacted and submitted suggestions and criticisms on the presentations that were being performed by other parents, thus

Interactive sessions during the conference (Photo courtesy of the Portuguese Haemophilia Society)

developing strategies for better communication.

The second workshop was about 'Legislation and rights' and the third one focused on 'Psychology and children with haemophilia', whereby using games we discussed important issues like adolescence, overprotection, the first years, transition to adulthood, how to deal with emotions, self-infusion, etc.

The second part was about scientific issues, such as types of treatment, novel therapies, inhibitors and prophylaxis. To talk about this, we invited three doctors who take care of children with haemophilia in treatment centres.

After the presentations, there was a fruitful dialogue in an informal environment between two essential parts of our community: doctors who, on a daily basis, deal with children and young people with haemophilia and their parents.

The main objective of this event was to help parents overcome fears and doubts, enabling parents and educators to better understand haemophilia. This aim was definitely achieved.

In conclusion, the event was very successful and the APH noted that many new parents need a platform to discuss and reflect on points related not only to the bleeding disorders of their children but also to other aspects such as social and psychological impacts.

The history of the Georgian Association of Hemophilia and Donorship

By Romanoz Khomasuridze, President of the Georgian Association of Haemophilia and Donorship

The Georgian Association of Hemophilia and Donorship (GAHD) was founded and established by Mr Temur Gholijashvili in 1990. He was the President of the association until his death in 2006. At that time, a few people who shared the same idea of the GAHD gathered, I was among them.

The idea for the establishment of the association was born when our country was a member of the Union of Soviet Socialist Republics (USSR). At that time, as you might be aware, Georgia was in the dark ages. We had no information about patients' associations in other countries. It was unimaginable for anyone in Georgia that either the World Federation of Hemophilia (WFH) or the European Haemophilia Consortium (EHC) existed.

Despite changes taking place in the USSR, the old bureaucratic machine was not facilitating the establishment of a social organisation such as a patient association. In 1991, we did not have any information regarding anti-haemophilic factor concentrates.

When the association was established, we registered 240 members. Today, we have 340 members. Our members are patients with haemophilia as well as patients with other bleeding disorders and their families. In 1992 we became a member of the WFH, in 1993 of the EHC.

In Georgia, there are one national and two regional haemophilia centres. The main centre is located in Tbilisi (the capital of Georgia), where new patients are diagnosed. The State Program for providing factor concentrates started in 2000 with an amount of 0.2 IU/capita and currently we have 1 IU/capita. However, to reach this result we had to resort to going on hunger strikes. We informed the WFH about the hunger strike and the then-President of the WFH, Mr Brian O'Mahony[6] and the then-Program Coordinator Mrs Claudia Black immediately came to Tbilisi. Their negotiations with the Georgian government completely changed the situation.

Members of the GAHD during the hunger strike in early 2000 to obtain better access treatment (Mr Khomasuridze is the third from the left on the first row - photo courtesy of GAHD)

Therefore on behalf of all the members of the GAHD we

[6] Mr Brian O'Mahony is now the President of the European Haemophilia Consortium.

would like to thank you all for your support.

Since 2002 there is a governmental programme, which supports hospitalisation and out-patient care for Georgian haemophiliacs.

Mr Brian O'Mahony (fourth from the left) in Georgia to negotiate with the government for better access to treatment (photo courtesy of GAHD)

The GAHD team is composed of:

- President: Mr Romanoz Khomasuridze
- Office manager: Mrs Evgenia Muzashvili
- Chairman of the Board: Mr David Bibichadze

We also have some volunteers, who support us in various activities. Unfortunately like many patients' association we have trouble to engage and retain our volunteers.

Georgia is considered as a centre for workshops held in the Caucasus region, which is comprised of Azerbaijan, Armenia and Georgia. The WFH recently organised a workshop on physiotherapy, which took place in Tbilisi in June 2014. We also participated in a rehabilitation workshop, which was initially organised by the Lithuanian Haemophilia Association.

Our association provides three main services to its members. The first one is the diffusion of information about the disorder. This is done by our members and staff by translating and printing literature. The second is the organisation of summer camps for children. These take place in resorts where participants receive treatment with a radioactive Radone baths, which provide very positive results. The third is to provide some financial support on a case-by-case basis to some of our members in need. We also provide financial support to our younger members to attend international conferences.

Funding of these activities is achieved by answering calls for tenders. We also receive some support through grants from pharmaceutical companies. The National Haemophilia Centre provided partial financial support for the summer camps as part of the rehabilitation projects.

Young members of the GAHD celebrating World Haemophilia Day in 2012 (Photo courtesy of GAHD)

Since the association no longer participates in public tenders, it will be very difficult to finance these projects in the future.

GAHD's proudest achievements lay in our contribution to secure state funding for haemophilia care and to increase factor concentrate use from 0.2 to 1 IU/Capita. We also feel that we have made great progress in developing a coordinated collaboration between the National Haemophilia Centre and the Ministry of Health.

In the future we would like to ensure that sufficient amounts of factor concentrate are purchased and that children can access prophylactic treatment. We will also strive to increase the involvement of younger member in the organisation's activities.

Serbian Haemophilia Society Profile

By Tatjana Markovic interviewed by Laura Savini***

In 2014 the EHC newsletter features a series of direct written and telephone interviews with representatives from NMOs. For this second edition, we interviewed Tatjana Markovic, Vice-President of the Serbian Haemophilia Society, who explains what have been the priorities of the Society. She gives a quick overview of the situation for people with bleeding disorders in Serbia and talks about future projects.

The Serbian Haemophilia Society was established in 2000 by a group of people with haemophilia and parents of children with haemophilia, together with Dr Danjela Mikovic and Ms Gordana Jankovic from the Blood Transfusion Institute, the Heamophilia Treatment Centre in Belgrade. The objective of the association was to improve the quality of treatment for people with bleeding disorders. The Serbian Haemophilia Society became a member of the EHC in 2002 and in 2015 it will not only celebrate its 15th anniversary but also host the EHC Conference in Belgrade.

> *"The Society was established because we did not have any institution, which would support patients and their needs. It was only people and as people alone we cannot act, so we needed to create an institution,' said Tatjana Markovic on the reasons to create the Serbian Haemophilia Society.*

She added that at the time of its creation cryoprecipitate was the treatment of choice for people with bleeding disorders and that factor concentrate was only administered in cases of intra-cranial or other life-threatening bleeds. Nowadays, the level of treatment has somewhat improved with FVIII concentrate levels per capita reaching 1.22 IU/capita in 2013 and an estimated 1.54 IU/capita in 2014. However, these levels are still below the recommended 3 IU/capita set as minimum standards by the Kreuth III recommendations (see article pg 12). Until the end of this year, the government has stated its intention to purchase additional quantities of factor. Also, a large number of patients with severe haemophilia are part of clinical studies and this helps to avoid severe shortages of treatment for the time being.

Besides advocating for the improvement of treatment levels, the Society also has a mission to provide advice, legal and social support to its members. This is done through the organisation of summer camps for children, which have been organised since 2003 and which have also been open for the past two years to patients affected by inhibitors. Another objective is to raise awareness about bleeding disorders with the general public. To do so, each year the Society organises events around World Haemophilia Day and has collaborated in the past with physicians to organise a country-wide media campaign, so that 'regular' people will learn about bleeding disorders.

Today, the Society has around 250 members and the country counts seven haemophilia treatment centres located in Belgrade, Novi Sad, Nis and Kragujevac, and in Itch. People with bleeding disorders in Serbia need to register as patients in the centralised registry (which has been in place since 1963); once that is done they can access treatment in 30 secondary care clinics located across the country. In general, it is always more difficult to access treatment towards the end of the year as stocks of factor concentrate run low.

Table 1: Recorded number of patients with bleeding disorders in Serbia	
Condition	Recorded number of patients
Haemophilia A	422
Haemophilia B	75
Von Willebrand Disease	259

The Society also works closely with other patient groups: it is a member of the World Federation of Haemophilia (WFH) and has been participating actively in the WFH Advocacy in Action Program and with a large number of workshops (e.g. in orthopaedics, dentistry, workshop for nurses and so on), which were organised in Serbia in the last 10 years. It is also an active member of the Association for Improvement of Clinical Tests in Serbia – KLINIS and it is an associate member of the Serbian National Organisation for Rare Diseases (NORBS).

The Board of the Serbian Haemophilia Society. From left to right: Stefan Dimitrijevic, Gordana Stevanovic, Vladimir Ilijin, Tatjana Markovic, Dejan Petrovic.

(Photo courtesy of the Serbian Haemophilia Society)

At the moment the primary goal of the Society remains to increase treatment levels for all patients, which is proving to be a difficult task mainly due to the lack of funding. In the long-term, however, the Society would like to focus on other projects such as establishing comprehensive care and prophylaxis for children. The Society also works closely with the Ministry of Health, the National Healthcare Insurance Fund and other healthcare institutions where people with haemophilia are treated.

The Serbian Society has the ambitious project to develop a three-day workshop aimed at 100 participants to provide scientific, psychological and advocacy training to its members.

The main difficulties faced by the association are similar to those of other organisations that relies on the work of volunteers. The Society does not have any paid staff and therefore its Board had to undergo a learning process to figure out the management of the Society and how to professionalise its work.

Finally, 'Tatjana describes the last ten year of her volunteer work as *hard-working, inspiring and motivating*. She is particularly proud of two achievements: the first one is the implementation of home treatment and the second one is the contribution to change mentalities *vis-à-vis* haemophilia and other bleeding disorders. Home treatment in Serbia is now possible but it took a good year and a half of advocacy and education to change the situation. As for the mentalities, for a long time there was a real stigma associated with bleeding disorders and people affected by them were not comfortable talking about their condition. However this is changing and this is also thanks to the collaboration with the Serbian Haemophilia Care Doctor Group who helped develop a media campaign to raise awareness about haemophilia and other bleeding disorders. Tatjana believes that patients need to stand up for themselves, gain knowledge about their rights and make their voices heard. In efforts to accomplish that, the patients and members of the Society have the constant support and assistance of the doctors, and only in cooperation with them the Serbian Society can improve the treatment of patients with haemophilia. She hopes that Serbia will one day have the same levels of treatment and care as more fortunate countries like Canada,' she concluded.

**Tatjana Markovic is the Vice-President of the Serbian Haemophilia Society*

***Laura Savini is the EHC Communication and Public Policy Officer*

Feature Articles

EHC Steering Committee Member attends Eurordis Summer School

Olivia-Romero-Lux interviewed by Laura Savini***

Olivia Romero-Lux, member of the European Haemophilia Consortium (EHC) Steering Committee and of the Association Française des Hémophiles (AFH – the French Haemophilia Society) had the opportunity and great pleasure to attend the summer school organised by the European Organisation for Rare Diseases (EURORDIS). She briefly describes the curriculum and why she believes every EHC NMO should apply to take part in this training.

Olivia first learned about the Eurordis Summer School through Thomas Sannié, President of the AFH, who suggested she attend the event. Olivia was uncertain at first of what to expect from this training but she came back with much enthusiasm and very positive feedback from the four-day course.

The Eurordis Summer School is a programme co-financed by the European Institutions and the AFM Téléthon, a French fund-raising event that takes place every first weekend of December.

Participants at the 2014 Eurordis Summer School (photo courtesy of Eurordis)

The idea behind the summer school is to train patients' representatives to one day sit on the various committees of the European Medicines Agency (EMA). In fact, many of the EMA committees have seats allocated to patients' representatives (see Table 1), so that they can provide advice and insight on matters such as clinical trials, product authorisation, paediatric medicines and so on. However, these committees are often very technical and in order to gather the best possible input from patients, Eurordis provides a training that helps patients' representatives understand how a medicine is developed and marketed from A to Z. For example, the training will teach participants about the different stages of a clinical trial, how to evaluate the quality of the data and the results generated by such trials, and how any medicine is assessed for its efficacy and safety before being authorised for the European Union (EU) market.

EMA committee with patients' representatives	Role
The Pharmacovigilance Risk Assessment Committee (PRAC)	PRAC is responsible for assessing and monitoring safety issues for human medicines.
The Committee for Orphan Medicinal Products (COMP)	COMP is responsible for reviewing applications from people or companies seeking 'orphan-medicinal-product designation.
The Committee for Advanced Therapies (CAT)	CAT is responsible for assessing the quality, safety and efficacy of advanced-therapy medicinal products (ATMPs) and following scientific developments in the field.
The Paediatric Committee (PDCO) – see page 21	PDCO is responsible for assessing the content of paediatric investigation plans and adopting opinions on them. This includes assessing applications for full or partial waivers and assessing applications for deferrals.
The EMA Human Scientific Committees' Working Party with Patients' and Consumers' Organisations (more commonly known as the Patients' and Consumers' Working Party or PCWP)	PCWP provides recommendations to the European Medicines Agency and its human scientific committees on all matters of interest to patients in relation to medicinal products.

Table 1: List of EMA committees with patients' representation

The latest summer school took place last June in Barcelona, Spain, and was attended by close to 40 participants from all over Europe. The training was given by members of the EU committees including the COMP, CHMP and PDCO as well as by representatives from Health Technology Assessment (HTA) agencies such as the English National Institute for Health and Care Excellence (NICE) and from Eurostat, the European Agency for Statistics. The issue of ethics was also presented and discussed.

"For me this training was an eye-opener. It really helped me to understand how the process of medicinal product development and marketing authorisation works. This is essential for a volunteer such as myself, as navigating this system is not always easy," she says. Olivia also noted that it really made her have a deeper understanding of the pressure applied by industry on regulators when they submit dossiers for evaluation. She noted that the role and impact of industry is much greater than the role of patients' groups, for which, for example, opinions provided while sitting on the EMA committees are not binding.

The workshop was preceded by a webinar, in which participants were provided with advance information on the training content and logistics. Participants were also convened for a follow-up webinar to gather feedback on the training and explore options on how to further use the training received.

One of the most interesting presentations was on HTAs. This was of particular interest in relation to the evaluation of upcoming longer-acting products for the treatment of haemophilia. Another fact that Olivia learned was that obtaining a centralised marketing authorisation for the EU did not mean that companies would actively market product in all 28 EU Member States, which is also something that limits patients' access to treatment.

Olivia also noted that haemophilia is quite ahead of the curve compared to other rare diseases in terms of treatment availability and medical and scientific expertise. She noted that unlike other rare diseases, haemophilia is not confronted to, for example, lack of treatment or subject to relying on a

single medicinal product. However, the haemophilia community is faced with other issues, including how to make treatment availability sustainable in the long term and everywhere.

Olivia also noted that a good command of English combined with an active participation and curiosity are essential for a successful participation.

"I urge all EHC NMOs to apply to this workshop through Eurordis, because it does provide anyone involved in patient advocacy with the right tools to carry out a more efficient and effective work and it facilitates networking," pointed out Olivia Romero-Lux

**Olivia Romero-Lux is an EHC Steering Committee member.*

***Laura Savini is the EHC Communication and Policy Officer.*

Treatment of Hepatitis C in Europe

By Declan Noone, Chair of the EHC Data and Economics Committee

Declan Noone is the Chair of the EHC Data and Economics Committee

At the World Federation of Haemophilia (WFH) Congress in Melbourne this year, Dr Michael Makris from the University of Sheffield and member of the EHC Medical Advisory Group, presented on the EUHASS[7] registry, which is now in its fourth year. The registry records adverse events in 75 Haemophilia Treatment Centres (HTCs) across 32 countries and represents 32,659 patients across Europe. The most striking comment was that the most common adverse event recorded was liver cancer and the most common cause of death was Hepatitis C (HCV)-related. This clearly shows the effect HCV is having on the haemophilia community across Europe. Whilst this is one of the first times we have seen this shown at European level, dealing with HCV and its consequences has been an increasing difficulty for the EHC National Member Organisations (NMOs). Until 2011, the only option available for treatment was pegInterferon (pIFN) and Ribavirin (RBV). This produced results in Genotype 2 and 3 of 70-80% cure and for Genotype 1 and 4 it was less than 50% cure. These were extremely difficult treatments to take, due to the side effects of treatment (headache, rash, fatigue, nausea, pruritus, anaemia, etc.) and the duration (24-48 weeks). The discontinuation rate due to side effects was approximately 20%. There are also several contra-indications to the use of this pIFN and RBV in certain cohorts such as depression.

In 2011, we saw two drugs come on the market (Telaprevir and Boceprevir). These were the first generation of Direct Acting Antiviral's (DAA's). However, they still had to be combined with pIFN and Ribavirin and were only effective against Genotype 1. The results increased the cure rates in Genotype 1 to 70-80%. The reported side effects also increased. It is important to note that even though this is a difficult treatment and a lot should be considered relating to the individual's lifestyle, these treatments work well and it is extremely possible to get through the treatment. In Ireland

[7] EUHASS is a pharmacovigilance program to monitor the safety of treatments for people with inherited bleeding disorders in Europe. More information can be found at www.euhass.org

there were 19 individuals that have gone through treatment and with the correct hospital, NMO and peer supports available, none have stopped treatment as a result of side effects.

In January 2014, Sovaldi® (Sofosbuvir) by Gilead received a licence for all genotypes in Europe and in May, Olysio® (Simeprevir) by Janssen, received a licence for Genotype 1 and 4. A third drug, Daklinza® (Daclatasvir) by Bristol Myers Squibb, is expected to be licenced for all genotypes in September 2014. These drugs can be used with pIFN and ribavirin with varying degrees of effectiveness similar or improving on the current treatments. These drugs can also be used in combinations with each other without pIFN to improve results. They are mostly still combined with Ribavirin but there is potential that this too will be dropped from the HCV regimens in the near future. In early 2015, another set of combinations is expected. These are a fixed dose combination of Sofosbuvir and Ledipasvir by Gilead for all genotypes and a 3-drug combination of ABT450/r, Ombitasvir and Dasabuvir by Abbvie for genotypes 1 and 4.

With almost all of these combinations, cure rates are between 90-100%, the side effects are significantly reduced and the duration of treatment has also been reduced to 12-24 weeks. This effectiveness is not just seen in the ease to treat groups. These drugs are as efficacious in people with rapid progression, cirrhosis and people who have previously failed treatment.

Also, while HIV needs to be considered for additional complications, such as faster progression of disease and potential antiretroviral therapy (ART) drug interactions, there is no difference in the results of how effective these DAA's are between co-infected patients with HIV and HCV compared to mono-infected patients.

Until the last few years, patients who had advanced cirrhosis, had been indicated for a liver transplant or are post-transplant and were generally ineligible for treatments. This was for a good reason as in almost all clinical trials with pIFN and RBV, the side effects are generally more prevalent and have a greater magnitude in patients with cirrhosis compared to those with no, mild or moderate fibrosis. With the new DAA's, the toxicity of the treatments is significantly reduced and the possibility to treat patients to prevent decompensation or cure the virus pre or post-transplant to improve the chance of the transplant working are a very real option. For pre-transplant patients, an initial study of the use of Sofosbuvir and RBV has shown that if the individual receives a minimum of 30 continuous days of treatment prior to transplant, the likelihood of reinfection of the new liver is significantly decreased.

In most people post-transplant as a result of HCV, the disease returns in around four to 12 weeks. In approximately 30% of these, the virus will come back rapidly with significant fibrosis within one year after transplant. These patients are at a higher risk of liver transplant rejection and survival rates fall significantly once cirrhosis has developed. In the compassionate use program, patients who had exhausted all treatment options and had poor clinical prognoses were granted access to Sofosbuvir prior to licensing. In 104 patients, preliminary cure rates were 62% for patients. In a phase II study, 34 post liver transplant patients with moderate fibrosis received a three drug combination (ABT-450/r, Ombitasvir, Dasabuvir) and RBV for 24 weeks. With 26 patients' finished treatment the cure rate is 96.2%.

At the European Association for the Study of the Liver (EASL) meeting in London this year, new guidelines for the treatment of HCV were recommended. They indicated that wherever possible, patients should be treated with DAA's. EASL is also encouraging European physicians to combine products from different pharmaceutical companies to achieve the most potent interferon-free

regimens. The guidelines make recommendations for all genotypes, and include all DAA's that are expected to be licensed in Europe during 2014. The guidelines recommend that the first-generation protease inhibitors Telaprevir or Boceprevir should be used for treatment of genotype 1 infection only when newer options are not available. For other genotypes, the combination of pIFN and RBV is described as `acceptable` where newer options are not available. The guidelines also reference the prioritisation of treatment. All previously untreated and treated patients with liver damage due to HCV should be considered for treatment. Treatment should be prioritised for patients with significant fibrosis and cirrhosis. Treatment is justified in patients with moderate fibrosis and in patients with no or mild fibrosis the indication for and the timing of treatment can be individualised.

"The availability of these new treatments for HCV will lead to major changes in the management of the disease. The ease of administration, short length of treatment and minimal side effects will probably mean that the vast majority will qualify for treatment. However, not all barriers to treatment will be lifted. The major limitation remaining will be economic," explains Declan Noone.

The guidelines have been printed online as the pace of change in the HCV treatment area is so fast and will be updated as soon as approval dates for new interferon-free combinations are known. These are likely to be reassessed in late 2014 or early 2015. The full guidelines can be downloaded from the EASL website: http://files.easl.eu/easl-recommendations-on-treatment-of-hepatitis-C/index.html

The current cost in the United States (US) of a 12-week regimen of Sofosbuvir alone is of US$84,000 or US$1,000 per tablet. In France, this cost is approximately €67,000 and €60,000 in Germany. A 12-week course of Simeprevir, another new drug in the US is $66,400. As many of these new regimens will require the combination of two or more drugs like these for a course of treatment, they may be considered as not cost-effective in certain situations.

There are several things that need to be considered. The first is the number of people you treat in a country. In France, between 5 and 7% of the HCV population is treated annually and 4 to 5% in Germany. Whilst these are still very low levels of treatment rates, models predict that even at these rates the levels of liver transplant, decompensated cirrhosis and liver cancer (HCC) will decrease, in France between 2015-2020 and in Germany between 2020-2025. Whilst many European countries even by 2030 will still continue to see a rise in all these areas, as well as the costs associated with them.

The second is that by the end of 2015 there should be around nine new drugs available with at least five combinations of these drugs by five companies for the treatment of HCV. With cure rates greater than 90% in almost all categories of people with HCV in these combinations the competition for market share should be significant, forcing prices down which ultimately will lead to more people being treated. Sofosbuvir, which could be the backbone for some of these combinations, at US $84,000 for a course of treatment for the drug alone could come under fire even sooner than that as negotiations are currently being held by the manufacture to sell in India and Egypt for US $2,000-2500 and US $900, respectively. This has led to push back by 14 European countries, so far, joining together to negotiate a reduction in the price. Other issues may be re-imports of drugs from these regions or health-tourism to these areas for treatment. From a European perspective, if there are significant differences in the prices for these new drugs within EU countries there may be the potential under the Joint Procurement Agreement of a European tender to purchase them on an EU

tender basis which could also significantly reduce the price. However this would be voluntary by each country.

Finally, these new drugs are currently expensive but even at these levels it still makes sense to provide access to those in need of treatment as soon as possible. With increased competition these prices will come down and hopefully lead to increased access in the long term, which is the aim of anyone working in the area of HCV treatment and potentially eradicate the virus in the near future.

World Federation of Hemophilia Congress 2014: 'Innovation in haemophilia treatment'

*By Giuseppe Mazza, EHC Steering Committee member**

Giuseppe Mazza

The current treatment for haemophilia patients is now being revolutionised. Some 20 years after the introduction of recombinant drugs, a new era of treatment is coming, which will be characterised by longer acting clotting factors, subcutaneously-delivered drugs and other innovative treatments.

During the 2014 World Federation of Hemophilia (WFH) Congress that took place in Melbourne, Australia, several speakers discussed the on-going clinical trials of longer-acting drugs across the world and the results are very encouraging.

Regarding longer-acting products**,** Alprolix (rFIX-Fc), a type of recombinant factor IX bioengineered by Fc fusion technique, and the likewise modified factor VIII product, Eloctate (rFVIII-Fc)2, the two longer-acting clotting factors that are already available in the United States and Canada, outperform the other available products by providing longer-lasting protection from bleeding.

Regarding subcutaneously-delivered therapies, Mr Tetsuhiro Soeda (Chugai Pharmaceutical Co.) updated the haemophilia community with recent results on their bi-specific antibody ACE910 (anti-factor IXa/X) that mimics FVIII function. Interestingly, the drug can be subcutaneously injected thus preserving the venous access and potentially facilitating adherence to treatment. Furthermore, the bi-specific antibody may be used as a treatment in patients with inhibitors because it is not recognised by the circulating FVIII-specific antibodies. However, to fully assess its safety and efficacy we will have to wait until completion of the clinical trials (phase I/II is now underway) but the preliminary results are very reassuring considering that the two main advantages of this innovative drug are: subcutaneous route of injection and its suitability for use in inhibitor patients.

The session with the largest audience was on 'Current status of Hemophilia Gene Therapy' chaired by Prof David Lillicrap (Queen's University). During this session, Prof Katherine High (Howard Hughes Medical Institute), Prof Amit Nathwani (University College London) and Prof Trent Spencer (Emory University School of Medicine) showed their latest results on cell and gene therapy confirming the feasibility of a long-term bleeding disorder partial correction for haemophilia A and B. In particular, gene therapy for the treatment of haemophilia B (as mentioned by Prof High and Prof Nathwani) showed its safety and efficacy in two-year clinical trials. Currently, there are mainly three clinical trials around the world: University College of London, Chatham Therapeutics/Baxter and Spark Therapeutics/ Children's Hospital of Philadelphia. Based on the results of these, the main disadvantage of the gene therapy is the immune response against the viral vector. This may limit both the viral entry into the target cells and their survival. However, there are on-going attempts to reduce the immunogenicity of the viral vector. On the other hand, there are several advantages of this treatment. Firstly, patients treated with the largest amount of vector may dramatically reduce

their standard prophylaxis. Secondly, the clotting factor activity remains elevated for more than two years after the treatment. Thirdly, in the United Kingdom the net savings made by the decrease in FIX use could be more than £1.5 million.

During the same session, Prof Trent Spencer (Emory University School of Medicine) presented his work on the treatment of haemophilia A using genetically engineered FVIII and lentivirally transduced Hematopoietic Stem Cells**.** The main concept of this therapy is to modify patients' cells carrying the mutation *in vitro* by viral and non-viral approaches. Thus, cell therapy could be a personalised treatment of congenital bleeding disorders, avoiding immune suppressor regime and overcoming several safety issues encountered with gene therapy.

Overall, the innovative therapies can provide safer and more efficient ways of haemophilia management but still require further assessment.

**Giuseppe Mazza is a Ph.D. student at the University College London - Institute for Liver and Digestive Health.*

New perspectives on blood and plasma safety and blood-borne pathogens at IPFA conference

*By Radoslaw Kaczmarek, EHC Steering Committee Member**

Radoslaw Kaczmarek

This past 21-22 May the International Plasma Fractionation Association (IPFA) and the Paul-Ehrlich-Institut (PEI) held the 21st International Workshop on Surveillance and Screening of Blood Borne Pathogens in Rome, Italy. Radoslaw Kaczmarek reports.

Despite a clearly defined topic, the keynote session was actually devoted to treatment rather than surveillance and screening whatsoever. No wonder! Because we are about to see another great progress in the treatment of hepatitis C. If approval of the first two direct-acting antiviral agents (DAAs) boceprevir and telaprevir shook the medical world; this and next year are bringing a true earthquake. Nearly a dozen new drugs will offer multiple new and even more effective treatment options: many of them achieve 100% cure rate while others are interferon-free, causing less severe adverse events and even proving suitable in cirrhotic patients. These new drugs can potentially shorten the duration of therapy down to six weeks. You can read more on these products in Declan Noone's article on page 33. Indeed, Prof Jean-Michel Pawlotsky from Henri Mondor Hospital in Créteil, France, opened his talk provocatively by stating: "HCV is an easy-to-cure virus," and I do not believe that anyone was left outraged after he finished, having been shown a mesmerizing set of clinical trial results.

Prof Jean-Michel Pawlotsky stated that: "HCV is an easy-to-cure virus."

Dr Harvey Alter from the US National Health Institute Clinical Centre and a renowned figure in science for being responsible for the discovery of the hepatitis C virus, addressed, in his hyped but brilliant presentation, the economic aspect of new treatments. Economic barriers are seen as potentially the major obstacle that may prevent patients from taking full advantage of these

developments. It is estimated that the cost of treating 3.2 million Americans at US$84,000/cure would be US$270 billion; roughly 10% of the total US healthcare budget. The cost grows 50-fold if we include 150 million infected individuals globally. Yet Dr Alter expressly stated that despite the high costs, all models show interferon-free DAAs therapy to be cost-effective because the treatment is short-term and curative in almost all patients. Also, it markedly reduces the national cost of treating cirrhosis and hepatocellular carcinoma, which is currently estimated to be between US$30,000-70,000 annually – this should be seen as an annual cost multiplied by five or ten per patient. Furthermore, it markedly reduces the need for liver transplantation, which is currently estimated at US$350,000/transplant, and prevents secondary transmissions that add to the disease burden.

During the session on advances in pathogen removal/inactivation, Dr Mikihiro Yunoki from the Hirakata Research Laboratory discussed the results of the study on differences between target and model viruses, which are used in manufacture of plasma-derived medicines. For technical reasons, manufacturers use model viruses that closely resemble human-specific pathogens to validate the viral inactivation and removal steps. Yet these species may still be different enough (e.g. they may show different heat stability) to make some validation results irrelevant and Dr Yunoki particularly reminded that model viruses for hepatitis A and E viruses and B19 parvovirus should be selected very carefully.

Data on hepatitis E virus (HEV) susceptibility to routinely use inactivation/removal methods are scarce and it raises some concerns amongst clinicians. HEV is a zoonotic species and animal husbandry seems the primary source of infections. The virus causes a self-limited acute hepatitis without progressing into a chronic illness. Dr Ines Ushiro-Lumb from the UK Health Agency Protection noted that the incidence of HEV infections in Europe has been growing recently and became an issue in blood safety. In April the European Medicines Agency issued a concept paper calling for intensification of efforts to fully characterize the pathogen and its implications for blood and plasma safety.

Presentation during the event

The majority of the session on the donor policy focused on the MSM's (men who have sex with men, a collective term to describe all males who engage in sexual activity with other males, regardless of how they identify themselves in terms of sexual orientation) eligibility to donate blood. There is a wide variation in how this controversial issue is approached, with indefinite deferrals for MSM in some countries and no deferrals in other. Discussion on which solution is better caused some commotion in the audience but no apparent consensus was reached.

In conclusion, the most rousing take-home message was conveyed during the keynote session and I hope that in the near future we will see more deadly diseases suddenly become not much harder to cure than the common flu.

**Radoslaw Kaczmarek is a PhD student at the Ludwik Hirszfeld Institute of Immunology and Experimental Therapy in Wroclaw (Poland)*

EHC representatives attend and sit on panel discussions at ECRD 2014

By Laura Savini, EHC Communication and Public Policy Officer

The European Conference on Rare Diseases and Orphan Drugs (ECRD) is an event that takes place every two years and is organised by the European Organisation for Rare Diseases (EURORDIS). The 2014 edition took place in Berlin, Germany from 8 to 10 May and was centred around: 'The Rare Disease Puzzle: Bringing the Picture to Life.' The event was attended by over 700 participants from 40 countries around the world. Participants represented the whole spectrum of the rare disease world and included representatives from the patient, medical and research community as well as government officials and the pharmaceutical industry.

The programme was comprised of six parallel sessions on:

- Improving healthcare services,
- Knowledge generation and dissemination,
- Research from discovery to patients,
- State of the art and innovative practices in orphan drugs,
- Emerging concepts and future policies for rare disease therapies,
- Beyond medical care.

The event was attended by both EHC staff and representatives from the Steering Committee (SC) as it was also combined with the General Assembly of EURORDIS, of which the EHC is a member.

Furthermore, Radoslaw Kaczmarek, member of the EHC SC also sat on the panel during a session on 'Rare diseases beyond medicinal products,' in which Mr Kaczmarek provided a patient perspective on the inclusion of patients in the development and use of medical devices. Panellists emphasized the fact that even in the area of medical devices often it was difficult to develop and commercialise a device because it was financially unattractive. This was illustrated by the case of Xeroderma pigmentosum, a genetic disorder in which an individual is unable to repair the skin damage from ultraviolet sun radiations and therefore cannot be exposed to any sunlight. In this instance, a French physicians described how in order to provide protective wear to his patients, he contacted the National Aeronautics and Space Administration (NASA) for the supply of some of the equipment used by astronauts in space such as helmets. This was because no commercial alternative was viable, not for lack of technology but for lack of economic benefit. All panellists strongly encouraged patients' organisations to get more involved in the area of medical devices as they are the primary users of such devices.

The remaining sessions were very informative and touched upon many topics of interest for the bleeding disorder community such as reference networks, patients' registries, orphan drug regulation, and orphan medicinal product reimbursement. Many of the sessions were also attended by officials from both national governments and the European Institutions, which meant that they were able to provide the audience with up to date information on many rare disease initiative and which led to some very fruitful discussions in terms of suggestions for improvement and actions for next steps.

From the conference it appeared that there is a real investment in rare diseases and a willingness to develop diagnostics and treatment for those conditions that have no access to treatment. There is also a lot that is done to further research and data gathering for rare diseases. However, it still seems that financing these projects remains a challenge, as often funding from government and EU Institutions is limited and once awarded cannot be subsequently renewed. This means that structures and procedures for running rare disease research projects are implemented but often there lacks a reflection on how these projects can be sustainable in the long term.

This is the same for funding of orphan medicinal products, not only in terms of research and development but also for reimbursement once the products are marketed. In particular this is also true when looking at off-label use, which is quite predominant in certain countries more than others.

In short the event was very educational and provided good opportunities for networking. The next ECRD will take place in 2016 in Edinburgh.

Patients and professionals agree on the future of hospital pharmacy

By Laura Savini, EHC Communication and Public Policy Officer

The European Association of Hospital Pharmacists (EAHP) is an association of 34 national organisations representing hospital pharmacists at European and international levels. Their objective is to represent and develop the hospital pharmacy profession within Europe in order to ensure the continuous improvement of care and outcomes for patients in the hospital setting. Earlier in 2013, the EAHP took on the ambitious project to develop a set of robust hospital pharmacy practice standards for Europe. The European Haemophilia Consortium (EHC) was asked to provide feedback on these statements as part of the stakeholder consultation process.

Radoslaw Kaczmarek, EHC Steering Committee member, supported the review of these standards in their early development. In his opinion, it was important for the EHC to become involved in this process because as he explains: "The degree to which hospital pharmacies are involved in haemophilia care varies greatly in European countries, but regardless of that I believe it is in our best interest to expose that particular stakeholder to our problems and to ensure that their terms of reference are well-aligned with our specific needs. Health and life of people with haemophilia too often depend on awareness to miss such opportunities."

These European standards derive from a 2008 conference of the International Pharmaceutical Federation (FIB), which started a Delphi consensus process to set global standards for hospital pharmacists' best practice. As each world region is quite different in terms of resources, practices and expertise, the EAHP initiated a European consultation to tailor these statements to European hospital pharmacists' needs. Physicians, nurses, patients and carers, who work closely with these stakeholders, were involved in the consultation process to provide their expertise and experiences with hospital administered medicines.

The standards are divided into six categories representing the many competences and aspects of the profession, such as:

- Selection, procurement and distribution,
- Production and compounding,
- Clinical pharmacy services,
- Patient safety and quality assurance,
- Education and research.

Plenary Session at the first EAHP European Summit (Photo Courtesy EAHP)

The standards were discussed and approved by 31 national hospital pharmacy associations, alongside 12 patient organisations (including the EHC), four nursing organisations and three doctors' organisations during the first European Summit held in Brussels in May and attended by over 100 participants.

Now that the standards have been finalised, they will be taken home by EAHP members to be implemented as best practice in their own countries. However, differences in national legislations and practices will need to be taken into account.

The complete statements can be found on the EAHP website at: http://www.eahp.eu/sites/default/files/files/European%20Statements%20of%20Hospital%20Pharmacy.pdf

The European Statements of Hospital Pharmacy include:

- All hospitals should have access to a hospital pharmacist who has overall responsibility for the safe, effective and optimal use of medicines.
- Hospital pharmacists should be involved in all patient care settings to prospectively influence collaborative, multidisciplinary therapeutic decision-making.
- All prescriptions should be reviewed and validated as soon as possible by a hospital pharmacist.
- Hospital pharmacists should play a full part in decision-making including advising, implementing and monitoring medication changes in full partnership with patients, carers and other health care professionals.
- Hospital pharmacists should have access to the patients' health record. Their clinical interventions should be documented in the patients' health record and analysed to inform quality improvement interventions.
- Clinical pharmacy services should continuously evolve to optimise patients' outcomes.

Dr Roberto Frontini, EAHP President said, "Through the new European Statements of Hospital Pharmacy, patients, hospital pharmacists and our sister healthcare professionals have set out a clear vision for what hospital pharmacy should be achieving in every European country. The task now turns immediately to implementation. EAHP will roll out a series of tools and initiatives to support the

achievement of the statements, but a major onus now falls on health systems to prepare the way for improvement as well. The positive support from patient organisations and other healthcare professionals assures us that the statements are a shared aspiration and provide a route towards continuously improving patient care within hospitals in every European country."

Subsequent to the Summit, EAHP have indicated to EHC that they remain open to ongoing engagement with patient organisations on how best to ensure the achievement of the statements, particularly in such areas as off licence use of medicine, management of medicines shortages, traceability and clinical trials.

PLUS involvement in ABO Risk-Based Decision Making for Blood Safety

By Laura Savini, EHC Communication and Public Policy Officer

The Alliance of Blood Operators (ABO) is a working group comprised of six blood systems from across the globe. These organisations include the Canadian Blood Services, America's Blood Centres, the American Red Cross, the Australian Red Cross Blood Service, the National Blood Service and the European Blood Alliance.

The ABO is currently developing a framework on how to deal with risk-based decisions for its membership. The framework is meant to provide guidance on how to evaluate and manage the risk, how to communicate and engage with stakeholders involved in blood donations. It also looks at risk assessment and tolerability. The framework follows the ALARA principle, which stands for 'as low as reasonably achievable'.

PLUS, the platform of plasma protein users, has been asked to take part in the consultation process for the development of this framework as it represents patients' groups relying partially or entirely on plasma-derived products.

Last June, the ABO held a meeting in London Heathrow Airport to present the first developments of the framework and to 'test' them with stakeholders.

Blood collection, in particular for the purposes of transfusion, is a very sensitive area with regard to health threats. In fact, blood components for transfusion have generally a short shelf-life, which means that they cannot undergo comprehensive testing before they are used. That is why there is great emphasis on donor selection and on risk-management in case of the contamination of the blood supply. This is less the case for plasma-derived therapies, which nowadays undergo longer manufacturing processes including viral inactivation and removal steps and are strictly regulated under the European Pharmaceutical Legislation.

Nonetheless, it was deemed important by ABO to have a guidance to help its members across the world. It is also considered that the framework, once in place, could be tailored to a particular region's needs and health threats.

Part of the framework is to deal with stakeholders involved in the blood collection, whether it is donors or patients and this is why PLUS was involved. The framework advises that while a blood operator is identifying, assessing and making a decision on a particular threat, it should continuously communicate with stakeholders about this in order to maintain confidence and enhance partnership.

This meant that one of the topics of discussions of the day was on how to identify stakeholders and how to engage with them.

The topic of blood and blood components safety and more generally the safety of substances from human origins has been a top priority for European regulators for the past 20 years. More recently, the European Commission has launched a Rapid Alert system for Blood and Blood Components (RAB) to be used by Member State Competent Authorities (NCA) for blood safety. This system allows NCAs to quickly exchange information on potential threats to the blood supply and take actions to avoid any contaminations of recipients of transfusions. RAB will complement national surveillance systems and will primarily focus on cross-border threats.

Young Member of the French Haemophilia Society goes on 7,000 km journey on a reclined bike

By Luc Breugnon interviewed by Laura Savini***

Luc Breugnon, a 20-year old Frenchman with moderate (4% FIX) haemophilia B has travelled some 7,000 km by reclined bike across ten countries[8] in two months. Here he tells us more about his experience and lessons learned.

"I've always had the travel bug. When I was 15 I went to Australia on my own," he says. Following the end of a contract in the construction industry, Luc decided to go off and travel in some less-familiar European countries. "I read a lot of travel accounts and decided that this time in my life would be a good moment to travel again. I decided to go towards some parts of Europe that I was less familiar with." He decided to use a reclined bike as transport method to travel at a more human pace. "I didn't want to take planes, trains, etc. I really wanted to be able to see more of the countries I was crossing and to meet people, and add the human contact to this trip," said Luc.

Luc Breugnon during his travel (photo courtesy of Luc Breugnon)

[8] France, Spain, Portugal, Italy, Slovenia, Croatia, Bosnia and Herzegovina, Montenegro, Albania and Greece.

So he started to plan his journey by visiting the website Eurovelo (http://www.eurovelo.org/) a website indicating bicycle-friendly routes across Europe. After a month and half of administrative preparation, he left in wintry February from his hometown of Nantes located on the northern French Atlantic coast.

His original travel plan involved six months of travel and a more comprehensive tour of Europe, however his trip was shortened due to the physical and mental intensity of the journey. “I have always been fairly fit and sportive, however I really had some difficulties in finding my rhythm during this trip. I was always torn between getting some distance done and taking my time and enjoying meeting locals and seeing more of the places I was travelling through. Also, it’s quite difficult mentally to be on your own all the time. You often wish there were someone with you to share what you are experiencing. If I had to do it again, I would make sure to have a travel companion.”

Luc spent most of his journey sleeping in the wild as he did here in Spain (Photo courtesy of Luc Breugnon)

So we enquired on what were his favourite countries and in fact it was a rather difficult question. “I loved Greece and Croatia for the landscapes and the views, it was beautiful to see the sea and mountains side by side. Ironically, these were also two of the most physically-intensive countries because of the continuous climbing. From a human contact perspective, I loved Spain in particular, even though I had some great encounters in other countries as well. It’s really difficult to pick only one place, as I had some pretty amazing experiences everywhere I went.”

Luc told us that the most difficult part of the trip was to deal with daily necessities such as planning for food and finding lodging. Throughout his travel Luc spent most of his nights in a tent set up in the wild (see picture above). Also, as he carried everything on his bike, it was sometimes tricky to plan for food as he needed to consume over 6,000 calories a day due to the physical effort but he also wanted to travel as light as possible. Other difficulties included packs of street dogs running after him in rural areas, the climate that could be fairly cold and wet, and the reaction of locals. He recalls, for instance, his crossing of the Balkan region where people were not accustomed to seeing a reclined bike. Car drivers would honk their support, which was obviously nice, but became tiresome in the long run. Other difficulties included, for example, the inability to communicate with locals:

“Not many people spoke English and so you get by with gestures, however you wish you could have more complex conversations, because you are already travelling alone.”

Luc recalled with affection a few particular moments and encounters from his trip. For instance, while travelling in Albania he could not take a mountain tunnel because bikes were not allowed in it. This would have forced him to climb up to 1,500 metres of altitude to continue his travel. On his way uphill he met a police patrol, who enquired where he was going and when he explained the situation, they offered to escort him through the tunnel so that he could avoid the very difficult climb. Another time in Spain, a couple of Roma saw him setting up his tent late at night in the wild. At the time temperatures were quite low and they brought him to a natural hot water spring where he could in fact warm himself up. "I also had some other completely unexpected experiences, such as a herd of bulls starting to run along me, when I was riding my bike," he explained. But primarily he said that the best part of the trip was the kindness expressed towards him by many people who offered him some lodging, food and moral support.

If he had to give some advice to people who were considering such a trip he would tell them to do a thorough planning of their trip and to take the physical and psychological difficulties of travelling on one own seriously. If he had to do it again he would go away for a week as a test and to get accustomed to this type of travel. One of the biggest difficulties he faced was to leave all his loved ones behind.

At the moment, Luc is not considering another cycling trip in the near future. However, he would like to travel by foot or by kayak in other regions of the world. Whichever new adventure he decides to embark upon, the EHC wishes him a good journey.

**Luc Breugnon is a young member of the French Haemophilia Society*

***Laura Savini is the EHC Communication and Public Policy Officer*

EUHANET haemophilia centre certification process

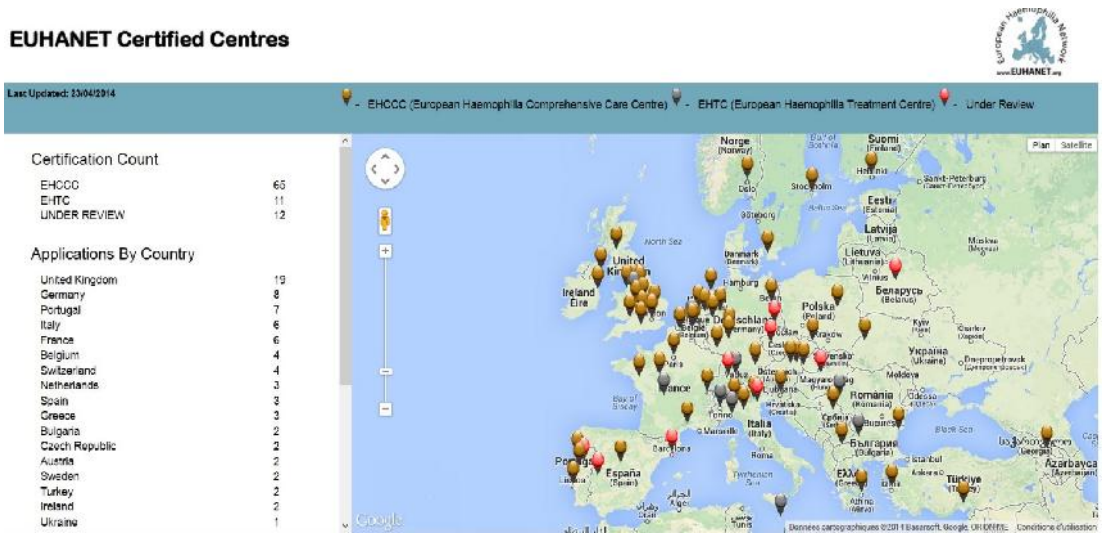
By Laura Savini, EHC Communication and Public Policy Officer

EUHANET is a project co-financed by the European Commission that encompasses four different components:

- **The Haemophilia Central Website** (see the EHC newsletter 2014/1).
- **The EUHASS website**, a pharmacovigilance program to monitor the safety of treatments for people with inherited bleeding disorders in Europe.
- **The Rare Bleeding Disorders Database**, an international database of rare bleeding disorders.
- **The Certification of European Haemophilia Centres.**

The Certification of European Haemophilia Centres

The certification of European Haemophilia Centres is a process by which haemophilia centres in Europe undergo voluntary certification to evaluate the level of comprehensiveness of the services they offer to their patients. This has the purpose to inform people with bleeding disorders regarding the services that a particular haemophilia centre offers. It was noted that in Europe there were great disparities and diversities regarding services offered by haemophilia centres, although they all tend to call themselves haemophilia centres, which is very confusing for patients when seeking healthcare services. This project aims at harmonising centres and classifying them into either European Haemophilia Comprehensive Care Centres (EHCCC) or European Haemophilia Treatment Centres (EHTC).



Screenshot of the EUHANET European Haemophilia Centre Certification Page

As the name indicates it, EHCCC offer more comprehensive services not only for medical specialties but also paramedical and laboratory services and in general have a greater number of patients and personnel. EHTC on the other hand offer a more limited service, which may be used for routine visits, counselling and less serious interventions.

At the moment the EUHANET Steering Committee is reviewing the applications and granting certifications based on the information provided in the application form. Currently independent auditing of these services is not organised.

Certification is seen as beneficial as a centre will be able to demonstrate more easily its specialisation and apply for additional funding in their country. However, the EUHANET does not provide any funding to the centre, once it certifies it.

Over 80 centres have been certified and the certification stage is due to be completed by May 2015, when the funding of the EUHANET comes to an end. The EHC and the EUHANET partners are currently planning how to proceed with this work after May 2015.

Announcements

Social media and EHC

Like us on Facebook : https://www.facebook.com/EuropeanHaemophiliaConsortium

We regularly update our Facebook profile with information about our activities and news from our members.

Check us out on YouTube : https://www.youtube.com/user/EHCTVChannel

You can find videos from our former conferences and more on our YouTube channel.

Events

October 3-5: EHC Annual Conference
Belfast, United Kingdom

More information about this event on www.ehcconference.org

Friday 3 October		
09.00-10.30	**WORKSHOP: Challenges in Mild and Moderate Haemophilia** *(Open to all delegates)* Facilitators: Dr Gary Benson and Thomas Sannié	
10.45-12.15	**WORKSHOP: Youth-Led Strategies for Engagement** *(Open to all delegates)* Facilitators: Amanda Bok and Michael van der Linde	
13.00-14.00	**Hepatitis: An Update** Chair: Brian O'Mahony	**NMO WORKSHOP: Haemophilia Treatment Centres and NMOs**

13.00-13.40	Update on Hepatitis C Treatment *Prof Geoff Dusheiko*	**Working Together** *(Open to NMOs only)* Facilitators: Dr Barry White and Tatjana Markovic
13.40-14.00	Follow up on Hepatitis C *Declan Noone*	
14.00-15.00	**The Role of Physiotherapy in Haemophilia** Chair: Prof Angelika Batorova	
14.00-14.30	Physiotherapy with Minimum Factor Availability *Piet de Kleijn*	
14.30-15.00	Physiotherapy with Optimum Factor Availability *Fionnuala Sayers*	
15.30-17.00	**Organisation Issues in Treatment** Chair: Gordon Clarke	**NMO WORKSHOP: Financing of Haemophilia Societies: a Survey-Based Workshop** *(Open to NMOs only)* Facilitators: Brian O'Mahony and Traci Marshall Dowling
15.30-16.00	Treatment Centre Certification *Prof Paul Giangrande*	
16.00-16.30	The Northern Ireland Comprehensive Care Model *Dr Gary Benson*	
16.30-17.00	The EU Cross-Border Healthcare Directive: One Year On Clinical View: *Prof Cedric Hermans* Patient View: *Radoslaw Kaczmarek*	
17.30-19.00	EHC Symposium 1 – sponsored by SOBI European Haemophilia Recommendations: A Debate with a New Generation	
19.30-21.00	**25 Years of the European Haemophilia Consortium** Welcome Reception and Buffet Dinner *Brian O'Mahony, EHC President* *Gordon Clarke, The Haemophilia Society UK* *Lord Mayor of Belfast* *Health Minister*	
Saturday 4 October		
08.30-10.00	EHC Symposium 2 – sponsored by BAXTER	
10.00-10.30	**Reproductive and Genetic Issues** *Prof Rezan Khadir*	

10.30-11.00	**Update: European Association for Haemophilia and Allied Disorders (EAHAD)** *Prof Philippe de Moerloose*
11.30-13.00	EHC Symposium 3 – sponsored by PFIZER
14.00-16.00	**Novel Treatment Products: Issues and Implications** Chair: Radoslaw Kaczmarek
14.00-14.30	An Update on Novel Treatment Products *Prof Paul Giangrande*
14.30-15.00	Individualisation of Therapy *Prof Claude Negrier*
15.00-15.30	Experience with the New Products To Date *Dr Beatrice Nolan*
15.30-16.00	Discussion
16.30-18.00	EHC Symposium 4 – sponsored by NOVO NORDISK
20.00-23.00	Tour of Titanic & Conference Dinner

Sunday 5 October	
09.00-11.00	EHC NMO General Assembly *(open to NMOs only)*
11.30-13.00	EHC NMO General Assembly *(open to NMOs only)*

October 6-8: European Patient Forum (EPF) Fourth Cross Border Healthcare Conference Tallinn, Estonia

More information on http://www.eu-patient.eu/Events/Cross-Border-Healthcare-Conference-6-8-October-Tallinn-Estonia/

When? 6-8 October 2014

When? Tallin, Estonia

Who can attend? Patient organisations' representatives from Denmark, Estonia, Finland, Latvia, Lithuania and Sweden. Further conferences will be organised in 2015 in other EU countries. In order to take full advantages of your participation at this event some criteria for participating have been defined, you will find them by clicking here: http://www.eu-patient.eu/Events/Cross-Border-Healthcare-Conference-6-8-October-Tallinn-Estonia/

What? With this conference, you will hopefully learn and share experiences about how the Directive works for patients and how you can contribute a strong patient's perspective.

December 1st: EHC Round Table on Haemophilia Councils Brussels, Belgium

On December 1st the EHC is organising a Round Table at the European Parliament on Haemophilia Councils. The programme, registration information and other logistical details will be shared soon on the EHC website and Facebook page.

December 1st: EHC 25th Anniversary Cocktail Reception Brussels, Belgium

Following the last Round Table of Stakeholders of 2014, the EHC will be organising a cocktail reception at the European Parliament to celebrate its 25th Anniversary. More information information on how to register and other logistical details will be shared soon on the EHC Website and Facebook page.

February 11-13: EAHAD 8th Annual Congress Helsinki, Finland

If you want your event to be featured in the EHC Newsletter, please contact Laura Savini at laura.savini@ehc.eu.