HAEMOPHILIA FOUNDATION AUSTRALIA

THE IMPACT OF HEPATITIS C UPON PEOPLE WITH HAEMOPHILIA AND RELATED BLEEDING DISORDERS

1. INTRODUCTION

Haemophilia Foundation Australia (HFA) will confine its submission to the *Committee of Inquiry into Hepatitis C and the Blood Supply in Australia (the Committee)* to a discussion about the impact of hepatitis C upon the haemophilia community. All references to haemophilia in this submission should also be read to include references to von Willebrand disorder (vWD) and related bleeding disorders unless express reference is made specifically to any of these. The submission relates to hepatitis C which has been medically acquired through the use of blood and blood products for the treatment of haemophilia and related bleeding disorders. Unless specified this submission does not extend to other modes of medically acquired hepatitis C transmission such as transfusion.

HFA expects that the Committee will have sought submissions from relevant experts to provide expert scientific, clinical and epidemiological data. HFA does not have the resources to conduct medico legal, scientific or epidemiological research, but must rely upon the integrity of such data from external sources. The strength of this submission will be that it will contribute relevant and valuable Australian and international experience about the impact of hepatitis C upon the haemophilia community.

In the submission HFA will address several of the questions of interest to the Committee of Inquiry, particularly the impact of hepatitis C upon the haemophilia community, the safety and supply of treatment products, the relevance of overseas experience and approaches to hepatitis C contamination in the blood supply, and the need for redress for people with haemophilia and von Willebrand disorder in Australia who have become infected by hepatitis C through blood products.

2. HAEMOPHILIA FOUNDATION AUSTRALIA (HFA)

HFA is the national peak body which advocates for the treatment and care needs for people with haemophilia and related bleeding disorders, including von Willebrand disorder and other rare factor deficiencies. Most services and activities are funded by donations, however the secretariat is funded by Commonwealth Department of Ageing. Its primary objectives are to represent people affected by bleeding disorders through advocacy, education and the promotion of research. HFA is governed by a Council of delegates from State/Territory Haemophilia Foundations.

The vast majority of people with haemophilia or vWD are treated at specialist centres located at major public hospitals throughout Australia. Haemophilia Foundations work closely with clinicians and health care professionals at these designated centres.

HFA has strong links with specialist health professionals groups, and auspicesand financially supports Australian Haemophilia Counsellors' and Social Workers' Group, HFA Nurses' Association and Australia New Zealand Haemophilia Physiotherapists' Group to enable them to develop specialist clinical expertise.

The HFA Medical Advisory Panel (MAP), whose members are haemophilia specialist clinicians from haemophilia treatment centres throughout Australia was auspiced and financially supported for many years by HFA. In 2001 MAP commenced operating as the Australian Haemophilia Centre Directors' Organisation (AHCDO) and this independent body is recognised as the peak clinical body that provides expert clinical advice and recommendations for the treatment and care of bleeding disorders in this country.

HFA hosts biennial national haemophilia conferences attended by people with haemophilia and other bleeding disorders, haematologists, infectious diseases specialists, liver specialists and other health care professionals, manufacturers, government regulators and policy makers. HFA is an active affiliate member of the World Federation of Hemophilia. Through its membership and work with this international body, HFA maintains up-to-date knowledge of the treatment of bleeding disorders and the complications of treatment including the management and care of blood borne viruses, blood product safety, and issues relating to the sustainability and supply of treatment products in both developed and emerging health care economies. HFA and its individual members are therefore very well informed about bleeding disorders and the complications caused by treatments, including blood safety and treatment product safety.

3. WHAT IS HAEMOPHILIA?

Haemophilia is a genetic disorder, which is usually inherited. The haemophilia gene is passed down from a parent to a child. Men with haemophilia pass the gene on to their daughters, but not to their sons.

Women do not usually have haemophilia, but they can be carriers of the gene. Women who are carriers have a 50 percent chance of having a boy with haemophilia and a 50 percent chance of having a girl who is a carrier. About one third of new cases are caused by a spontaneous mutation of the gene, which means that there was no history of haemophilia in the family before.

Haemophilia A or Classical Haemophilia, is the most common form of haemophilia and is due to the deficiency of factor VIII. Haemophilia B or Christmas disease is due to the deficiency of factor IX. The severity of haemophilia is determined by the level of clotting activity of factor VIII or factor IX in the blood. There are three levels of severity: mild, moderate, and severe.

The incidence of haemophilia is 1 in 6000 -10000 people. Prevalence is harder to determine as many people with haemophilia in developing countries are not diagnosed and without treatment die from haemophilia at an early age.

People with severe haemophilia bleed frequently into their muscles or joints. They may bleed one to two times per week. Bleeding is often spontaneous, which means the bleeding just happens with no obvious cause. People with severe haemophilia will have used large amounts of clotting concentrates for their treatment throughout their life

People with moderate haemophilia bleed less frequently, usually after an injury, perhaps once a month. Cases of haemophilia vary however, and a person with moderate haemophilia may also bleed spontaneously.

People with mild haemophilia usually bleed only as a result of surgery or major injury. They may never have a major bleeding problem.

4. WHAT IS VON WILLEBRAND DISORDER?

von Willebrand disorder (vWD) is an inherited bleeding disorder. It is the most common inherited clotting disorder, affecting both men and women. It has been estimated that vWD affects up to one percent of the whole population. However, it is generally the least severe of the clotting disorders.

vWD is caused by a deficiency or defect of a blood clotting protein called von Willebrand factor (vWF). This glue-like protein that helps platelets in the blood stick together and seal off tears in injured blood vessels. This is called a platelet plug. If a person does not have enough von Willebrand factor or it does not work properly, no platelet plug will form and bleeding will continue for a longer period of time.

Most people with vWD will have few, if any, symptoms and most will not require treatment unless having dental work or surgery. The main symptoms are easy bruising, frequent or prolonged nosebleeds, heavy or prolonged menstrual bleeding, and prolonged bleeding following injury, surgery, dental work, or childbirth. Treatment will be required for more severe forms of vWD with desmopressin (DDAVP) or with infusions of a clotting factor concentrate that contains vW factor. People with severe forms of vWD will have used large amounts of clotting concentrates for their treatment throughout their life.

5. TREATMENT

Haemophilia is treated by replacing the missing clotting factor in the blood. The necessary clotting factor must be injected into a vein. Bleeding stops when sufficient clotting factor reaches the bleeding site. When bleeding is into a joint it is very important that treatment is given as quickly as possible to prevent long-term damage.

Haemophilia is a lifelong or chronic condition, however the development of clotting factor concentrates has meant in most cases, that haemophilia can be managed effectively with proper treatment.

A small number of people with haemophilia develop inhibitors to clotting factors and bleeding continues unabated resulting in significant disability, particularly in adult haemophilia patients who have not had the benefit of sufficient quantities of inhibitor treatment products. Whilst children with inhibitors are more likely to be treated optimally in this country, adults with inhibitors still do not have access to the best product for this, (recombinant factor VIIa) except in the event of a life or limb threatening bleed. These people suffer from terrible ongoing pain and disability.

Today most people treat themselves at home. Timely treatment to stop bleeds enhances self care and independence, and helps reduce major joint damage/atrophy. Most people have normal life expectancy unless complications occur. Children are treated prophylactically, usually 2-3 times per week to prevent bleeds from occurring or to reduce their severity. In Australia, government policy has restricted preventive or prophylaxis to children on the grounds of cost. Nevertheless, there is strong argument that adults should also have access to prophylaxis.

Factor concentrates have revolutionised haemophilia treatment. They can be made from human blood (called plasma-derived products) or manufactured using genetically engineered cells that carry a human factor gene (called recombinant products). There are several levels of purity (the concentration of factor) ranging from intermediate to very high depending on the manufacturing process.

Synthetic or recombinant factor VIII does not contain von Willebrand factor and is not effective for the management of von Willebrand disorder, so this group of patients must use plasma derived concentrates which contain von Willebrand factor.

In the past, bleeding has been treated with unrefined blood plasma in the form of fresh frozen plasma or cryoprecipitate. Whilst generally effective to stop bleeds, and with the advantage of being made from small pools of blood they meant exposure to less donors which was an advantage. These products were sometimes used in preference to large pool products when it became known that blood borne viruses were infecting these products. This in fact did protect some people who were treated in this way in the lead up to viral inactivation techniques.

Concentrates by definition are preparations made by pooling blood plasma of many blood donations. Large pools increase the risk of infectious agents. Measures must be taken to reduce the risk inherent in the collection and viral inactivation processes used.

The therapeutic safety of plasma derived products depends on the methods used to prevent, remove, or inactivate viruses that may be present in the source plasma. The safety of plasma derived clotting concentrates is dependent upon donor selection, plasma pool size and the fractionation procedure and the associated viral inactivation processes.

Viral inactivation processes are based on heat, solvent detergent or filtration. Heat inactivates viral proteins and nucleic acids and prevents replication and can be used in dry preparation or in liquid (pasteurisation). Solvent detergent inactivates enveloped viruses such as HIV, hepatitis B and hepatitis C and makes them non infectious, but it is unsuccessful against non enveloped viruses such as hepatitis A and parvovirus B19. [1]For this reason plasma derived products with two effective viral inactivation steps, including one that is effective against non enveloped viruses are considered safest.

There is great reliance on the scientific and regulatory community to ensure current viral inactivation procedures used in the fractionation of products are sufficient to eliminate the risk of transmission of known viruses. Regulators are quick to point out that it is impossible to achieve zero risk, and there is always the potential for an unknown agent for which screening and blood testing may be ineffective or for human or manufacturing error to occur.

6. CHRONICITY OF HAEMOPHILIA AND DISABILITY

There is no cure for haemophilia. Gene therapy promises hope for the future, however experts consider it will be at least 20 years before the scientific, clinical, ethical and other barriers will have been removed to enable safe, effective and accessible treatments to overcome the burden of haemophilia. A recombinant clotting treatment product for the management of inhibitors is available to children in Australia, however product access for adults is only available to adults if they are experiencing life or limb threatening bleeds. HFA considers that inhibitor treatment in Australia is sub - optimal currently for adults.

Medical and technological progress in recent decades means it is now possible to manage and prevent the complications of haemophilia. Clotting factor can be made safer than ever before. The quality and safety requirements of key regulatory authorities continue to strengthen standards. Today, improved treatment knowledge with new modes of treatment, including prophylaxis as standard treatment are proven to be extremely effective and prevent long term joint damage and disability.

However people with haemophilia nevertheless live with the legacy of past treatments and the effectiveness and safety of those treatments. Many are crippled with disabling and painful arthritis. Even with current treatment, many adults have to struggle to maintain an adequate

quality of life. Many suffer as a result of inadequate treatments. Haemophilia continues to be a challenge as it requires treatment for life and it presents complex medical and psychosocial issues for the individuals affected and their families. The memory of past experiences of poor treatment, inadequate treatment products, and the tragedy of HIV/AIDS followed by hepatitis C and the perception that blood borne viruses could have been prevented results in distrust, pain, grief and fear for many. [2]

Inadequate supply of safe clotting factor treatments puts people with bleeding disorders at risk of life or limb threatening consequences. In a health care economy such as Australia, mortality or morbidity due to inadequate treatment is unlikely and is unacceptable, however without appropriate measures in place to ensure an adequate supply of the safest treatment products people with bleeding disorders will continue to risk unnecessary iatrogenic consequences of their treatment.

……..canaries in the mineshaft……..

People with bleeding disorders requiring blood clotting agents to stop their bleeding, throughout the world, have always been amongst the first to be affected when a virus or pathogen has entered the blood supply because of the lack of, or inadequate blood screening measures or viral inactivation processes.

Australia is no exception to this and the hereditary nature of bleeding disorders is such that most families with haemophilia have one or a number of members infected with either HIV and or hepatitis C. Many of their relatives have died, whilst others must live with the health, psychosocial and financial consequences of the use of unsafe blood products prescribed for their treatment. They continue to live with physical disability and pain of chronic arthritis caused by prolonged bleeding into joints and muscles.

Despite the various risk management approaches implemented over the years to make the blood supply safer, including donor screening, donor deferral, NAT testing, and viral inactivation procedures to treat fractionated products, it is only a matter of time that those who are dependent upon these clotting concentrates for their treatment will again be failed.

7. HEPATITIS C IN THE HAEMOPHILIA COMMUNITY

Following treatment with contaminated blood clotting factor concentrates given as part of their treatment provided by the Australian Health Service, 85-90% of people with haemophilia have been infected with hepatitis C. It is likely that up to 90% of people with haemophilia A and haemophilia B developed non A non B hepatitis (NANB hepatitis) with their first treatments of non heat treated clotting factor.[3] More than 250 people with haemophilia were also infected with HIV and many of these people also have hepatitis C.

8. HOW MANY PEOPLE IN AUSTRALIA ARE INFECTED WITH HEPATITIS C IN AUSTRALIA?[4]

It is unfortunate that there is no comprehensive data available on haemophilia, vWD and hepatitis C in Australia. AHCDO collects data for the Australian Bleeding Disorder Registry (ABDR), however this does not contain data for NSW. HFA has access to limited unpublished ABDR data and the Senate Community Affairs Legislation Committee published Questions on Notice Question

ABDR (all States except NSW)

446 people with haemophilia have hepatitis C (79 also have HIV)

82 people with haemophilia B have hepatitis C (5 also have HIV)

64 people with vWD have hepatitis C (3 also have HIV)

Total number of people on the registry = 1769

However a further 395 have no hepatitis C status recorded. Assume 50% have hepatitis C, a further 197 = 789

NSW

225 people out of a total of 748 reported to have hepatitis C, however as this may exclude vWD,add a further 3.6% in line with proportion of vWD patients with hepatitis C in ABDR (8 patients) = Total of 233 in NSW with hepatitis C

APPROXIMATELY 1022 WITH HEPATITIS C

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9. BLOOD SAFETY

"Safety of the blood supply system is paramount. The goal of the blood supply system must be to supply safe therapies to persons who need them. The principle of safety must transcend other principles and policies.

The costs of promoting safety may well be high – for example when new pathogens appear and new tests are required, when newer and more sensitive tests are developed to identify known pathogens, or when blood products must be withdrawn or recalled and be replaced because they are or may be unsafe, the promotion of safety may well require that substantial sums of money be spent. When enhanced donor screening measures are needed to identify a new pathogen, the cost to the blood supply system may be a reduction in the number of donors.

The safest blood supply is an aspect of public health philosophy, which rejects the view that complete knowledge of a potential health hazard is a prerequisite for action. *The balancing of risks and benefits of taking action should be dependent not only on the likelihood of the risk materialising but also on the severity of the effect if the risk does materialise, on the number of persons who could be affected and on the ease of implementing protective or preventive measures. The more severe the potential effect, the lower the threshold should be for taking action.*

Preventive action should be taken when there is evidence that a potential disease causing agent is or may be affected. ***If harm can occur, it should be assumed it will occur.*** *If there are no measures that will entirely prevent the harm, measures that may only partially prevent transmission should be taken".*

(Krever) [5]

HOW DID IT HAPPEN?

10. TESTING OF BLOOD

Hepatitis has been known for many years. The link between jaundice and liver problems was known despite there being no identified causative agent which could be tested for and the problem of post transfusion hepatitis was also well known. The hepatitis B surface antigen (HBsAg) was identified as part of the hepatitis B virus and allowed for tests to be developed to screen blood for hepatitis B in the 1960s. A test also became available for hepatitis A antibodies in 1973. Despite the expectation that these tests would identify most cases of serum hepatitis (hepatitis B) and infectious hepatitis (hepatitis A), they did not. However, significant numbers of cases of hepatitis were caused by neither hepatitis A and hepatitis B. This was called non A non B hepatitis (NANB). There was no test for this until 1990, after the hepatitis C virus was cloned by Chiron in 1989. This antibody testing showed that hepatitis C had been the cause of NANB hepatitis and liver disease. In the mid – to – late 1970s it was accepted that transfusion of blood could cause NANB hepatitis in recipients.

By the early 1980s it was apparent that most people infected with NANB hepatitis were carriers and could transmit the disease by exposing others to their blood. People at risk were recipients of blood transfusion, people who had used intravenous drugs (shared needles) and

people who engaged in behaviours where blood contamination was possible (tattooing) and people with previous episodes of jaundice or liver problems.

NANB hepatitis was recognised as a cause of long term health effects by the early to mid 1980s, even though in most cases identified there were no symptoms associated with initial infection.

Many people with haemophilia in Australia have been aware of their “funny liver levels” since the 1970’s and were known to have NANB hepatitis from the use of blood products and any symptoms they had “were lived with”. Many did not experience any serious symptoms. The risks inherent in plasma pooling were balanced against the benefit of the utility of concentrates. Hepatitis was seen as an unfortunate consequence, but an acceptable risk of blood products.[6] Some patients were spared through the use of cryoprecipitate which they continued to use until testing. Nevertheless for many, it is likely that hepatitis C antibody positive donations have been a part of every plasma fractionation pool since 1952 when the process commenced.[7] After the first generation antibody test became available many haemophilia patients received letters from their clinicians to inform them that they had tested positive for hepatitis C soon after the test became available , but they were advised that they did not need to worry about it as “hepatitis is a benign infection”.

In reality, people with haemophilia had no choice of whether or not to use plasma products. When they have severely painful joint or a life threatening bleeding episode, the decision is clear to use the available treatment products, even if the treatment may have associated risks. Living with recurrent and chronic pain is very difficult.

There was great trust placed in products that were developed to treat bleeds, but little was known about their safety risks until HIV came through the blood supply. Parents continue to live with the guilt of having treated their children with these infected products.

A key issue is whether adequate screening of blood donors was undertaken to identify donors for risk factors of infection with NANB hepatitis and whether blood which showed elevated ALT levels (a possible sign of NANB hepatitis) or anti-HBc (indication of past infection with hepatitis B) should have been discarded (surrogate testing). Most people with haemophilia were exposed to many donors, and have an increased likelihood of having been exposed to more than one infected donor.

11. SURROGATE TESTING

The use of surrogate testing to reduce transmission risk has always been controversial in Australia as it was in the USA and elsewhere between 1981 and 1983.

Testing clearly reduced the risk of transfusion transmitted NANB hepatitis in some donor populations before hepatitis C tests were available and these markers had been helpful in reducing the risk of transmitting NANB hepatitis via some donor populations.[8] In Australia surrogate markers were only adopted to screen blood in Queensland, however it is unclear whether studies of comparable donor populations to measure the effects of this factor were undertaken.

The benefit of surrogate testing appears to have been balanced against other issues. Despite the international debate, there was local concern that NANB hepatitis was less prevalent in Australia and that surrogate testing would jeopardise the local blood supply. We understand the Australian Red Cross Society (ARCS) decided not to introduce surrogate testing pending a study into the incidence of post transfusion NANB hepatitis in Australia and the effectiveness of surrogate testing in Australia. An exception was the Queensland Division of the ARCS, which introduced ALT testing in mid 1987, but not anti-HBc testing. There is

debate about the actual efficacy of surrogate testing to detect NANB hepatitis. It is unclear just how many people may have been unnecessarily infected with hepatitis C through blood transfusions because of a failure to implement surrogate testing.

The Krever Commission was critical of Canadian blood services for long delays relating to screening. The Canadian investigators concluded that "although ALT screening lacks the sensitivity to detect all infectious units and lacks the specificity to detect only infectious units, the high correlation between an elevated ALT level and infectivity of transfused blood provides a compelling argument that such screening should be instituted". [9]

Krever wrote "the Red Cross (Canada) had said until the mid to late 1980's NANB hepatitis was believed to be a mild disease, yet by 1980 some studies had shown that between 25 -50 per cent of persons infected with NANB hepatitis had prolonged abnormal levels of ALT, and that of this group the majority showed evidence of chronic active hepatitis and 10-12 % showed evidence of cirrhosis. However little attention was given to the data demonstrating the serious consequences of NANB hepatitis until 1984 when a study at the US NIH found that as many as 20 %of patients with chronic NANB hepatitis developed cirrhosis. By the mid to late 1980's, NANB hepatitis was known to cause serious disease, including cirrhosis and liver cancer in a significant proportion of infected individuals. The seriousness of NANB hepatitis was one of the reasons that surrogate testing was implemented in the US". [10]

Krever was scathing about the lack of follow up and action in Canada despite the debate (p635) and the failure to resolve this issue "whilst some USA blood centres did implement ALT testing, in Canada the recommendation that a study of the incidence of post transfusion hepatitis or the desirability of surrogate testing for NANB hepatitis does not appear to have been followed up". Surrogate testing was rejected in Canada in favour of a multi centre study which was delayed for several years, but which showed on completion (by which time a test for hepatitis C was being used), that surrogate testing would have reduced post transfusion NANB hepatitis.[11]

In 1986 a blood products advisory committee of the United States FDA decided that both ALT and anti-HBc testing should be implemented, and although several blood banks in the US moved to adopt the tests in late 1986/87, the FDA did not issue a regulation requiring anti-HBc testing of donated blood until 1 March 1991 for the purpose of identifying units contaminated with HBV, and never issued a regulation requiring testing for ALT levels. Nevertheless by the end of 1987 all plasma intended for fractionation was being routinely tested for ALT levels in the USA.[12]

Other international responses to the question of surrogate testing were varied. For example, the German regulatory agency required ALT testing of all plasma used in clotting factor concentrates and would only accept plasma with ALT levels of less than twice the upper limit of normal. US companies that supplied concentrates to Germany therefore tested some plasma to German standards and used any that tested between 2-5 times the upper limit of normal for manufacture of products to be used elsewhere. Any plasma greater than 5 times the upper limit of normal was discarded and donors were deferred until ALT levels fell to below two times the upper limit of normal. Krever notes this was "clear acknowledgement of the risk, but they were still only testing a proportion of the plasma they were fractionating. Canada which was supplied from the USA, opted for plasma which was unscreened for ALT rather than the remaining plasma from that which was sent to West Germany". [13]

Krever reported, that "German blood centres began the ALT testing of donations as early as 1968. In July 1985 ALT testing was required of all plasma used in the manufacture of imported blood products. Germany did not require anti-HBc testing, but its efficacy was demonstrated in at least one study and some blood centres conducted anti-HBc testing voluntarily. ALT testing was also required by regulation or conducted routinely in Japan,

Switzerland, Spain, Italy, Portugal, Finland and Malta. ALT testing was conducted voluntarily in some blood centres in Australia, Belgium and Luxembourg".[14] It was not adopted in the UK on the grounds of the low incidence of NANB and cost effectiveness.[15] Barraclough refers to the UK which also did not implement surrogate testing because of the low risk of transmission of post transfusion hepatitis. Astoundingly, the UK blood bankers also questioned the need for antibody screening when it became available. ALT and anti-HBc screening was introduced in 1987 in USA.

Surrogate testing was not conducted routinely in Australia. Barraclough does not make an assessment of whether this was an appropriate strategy or not .[16] He does however refer to conflicting advice about the best course of action. The Ismay et al study (1995) suggested surrogate testing of donations by ALT or anti- HBc offered no advantage, however the Hyland et al study (1988) in Queensland concluded that the chronic effects of NANB hepatitis outweighed the argument against implementation of surrogate testing. Surrogate testing was adopted in Queensland.

Surrogate testing was introduced in Queensland in 1987, but not in other States. The debate was that whilst they reduced hepatitis transmissions, surrogate tests lacked sensitivity and specificity and would identify many false positives. Instead, the low incidence of post transfusion hepatitis and donor screening which had already been introduced to identify those at risk of transmitting HIV was relied upon elsewhere in Australia.

In 2001, Wood, Coghlan and Boyce[17] suggested that surrogate tests had been shown to be helpful in reducing the risk of transfusion transmitted NANB hepatitis in some donor populations before(sic) assays became available , but "their continued value in donor screening in the setting of current hepatitis C testing schedules is unclear. Many feel they provide some extra measure of safety, reflecting past risk behaviours of donors that may not otherwise be identified, although there is scant evidence to support this view. Others believe that surrogate tests are now unhelpful – deferring many donors for no defined medical reason, compromising the sufficient supply of blood products and creating significant anxiety and uncertainty in unnecessarily deferred donors. Furthermore substantial financial and human resources are devoted to initial surrogate screening, retesting and counselling donors with positive results on such tests, both by the blood service and during their consequent medical investigations and evaluations. Many would argue that these resources could be better spent ".This might well be a suitable argument in the presence of well developed antibody tests and other tests such as NAT testing, however such opinion which might also have been prevalent in the mid to late 1980's in the absence of antibody testing, may well have compromised the safety of patients at the time when it could have been avoided. If any kind of testing was available that could have potentially saved people from a life threatening virus, efforts should have been taken to implement these. Decisions based on cost effectiveness do not stand the test of time.

The adoption of surrogate testing by authorities in Australia prior to hepatitis C antibody testing would have been of concern at the time because of the cost of implementation, the impact on donors, a possible loss of public confidence in the blood system and the impact a loss of donors would have had on the supply of blood products, perhaps less of an issue if there were more blood donors. Krever said that the Canadian Red Cross was "convinced the cost of surrogate testing outweighed the benefits of testing despite contrary published evidence. ….it did not take into account the medical and social costs…… and therefore the savings that could be achieved through testing." [18]

It is a widely held view that the majority of people with haemophilia who became infected did so in their earliest treatments with pooled plasma derivatives and that ALT testing alone would not reduce the risk of NANB transmission, but combined with the viral inactivation procedures, including solvent detergent and heat treatment the risk may have been reduced.

Because of the large pool size used for the manufacture of fractionated products the viral inactivation steps are relied upon to eliminate the risk of viruses. Nevertheless, it is possible that if NANB hepatitis had not been considered such a benign disease by researchers, clinicians and policy makers, and if surrogate testing had been implemented universally some infections might have been prevented. If not in users of fractionated products, most certainly in those who had transfusions. People with haemophilia who had become newly infected with hepatitis C during the period of debate may well have avoided that infection had surrogate testing been implemented.

As patient records are likely to be poor it is difficult to know how many people became transmitted NANB hepatitis in the period when surrogate testing was being debated and thus the consequence of hepatitis C might have been avoided for a small group. [19]

12. TREATMENT PRODUCT SAFETY HISTORY

There have been several instances where Australian haemophilia treatment product safety has been at risk. HFA can only refer to specific events of which it is aware to demonstrate this problem. Barraclough was charged with the responsibility to investigate whether hepatitis C positive plasma was used in the manufacture of plasma products for several months in 1990.[20]

In his Executive Summary pp 1 – 4 he writes that:

Australia was one of the first countries in the world to introduce the first generation hepatitis C antibody test for donation of blood and plasma in order to increase the safety of the national blood supply…….

In 1988–89, before the introduction of the first generation hepatitis C antibody test, the overall risk of post-transfusion hepatitis was approximately 1 per cent. This was almost half that of a decade earlier, an improvement attributable to changes in donor screening and transfusion practices and in the donor population in the wake of the HIV pandemic.

The first generation hepatitis C antibody test identified about 85 per cent of potentially infective donations. However, it was also known to give a high level of false positive results. It has subsequently been estimated that only approximately 30 per cent of donations of blood or plasma that tested repeatedly positive to the first generation hepatitis C antibody test would actually confer risk of transmitting virus to the recipients.

There was significant divergence of scientific opinion and debate internationally during the early part of 1990 about the relative safety of immunoglobulin manufactured from plasma that did not contain hepatitis C antibody as compared to plasma containing anti-hepatitis C antibody.

Based on the incomplete scientific knowledge of the time, and after wide consultation and detailed discussion on the conflicting evidence by committees of experts, the decision was taken to allow plasma that tested positive to the first generation hepatitis C antibody test to be sent to the Commonwealth Serum Laboratories from February 1990 and further decisions were taken in July 1990 that stopped its use.

This plasma was available to be used in the manufacture of plasma proteins that were known to be safe and not to transmit hepatitis C, provided proscribed viricidal manufacturing processes were followed. It was not to be used for the manufacture of Prothrombinex (Factors IX and X) and Factor VII, where the viricidal processes were

necessarily less rigorous and therefore less effective.

It is probable, but not certain, that some of the anti-hepatitis C positive plasma sent to the Commonwealth Serum Laboratories was actually used in the routine manufacture of albumin and immunoglobulins, but it is less certain that this plasma was used in the manufacture of Factor VIII product.

Donors whose blood repeatedly tested positive to hepatitis C screening tests were told they could continue to donate blood for the manufacture of plasma fractionation products only until July 1990, after which blood banks were advised that this practice was to stop. Donors were not finally deferred from donation until tests that could confirm their hepatitis C status became available. Such tests became available from September 1990.

From July 1990 until July 1991, some plasma testing hepatitis C positive was sent to the Commonwealth Serum Laboratories for segregated storage with a view to future use in the development of a new hyperimmune anti-hepatitis C immunoglobulin, but with clear instruction for it not to be used in manufacture of other products. This program was never initiated and the plasma sat in safe storage. Any remaining stored hepatitis C positive plasma was destroyed by May 1994.

Decisions to exclude donations of plasma that tested positive for hepatitis C from the manufacturing process for fractionated plasma products were taken in June and July 1990. They were taken after international and local scientific debate and in recognition that safety was likely to be enhanced if the possibility of human errors in labelling, transport, storage and manufacture were reduced by excluding these donations. The science relating to the decision was still not clear, but arguments against the use of anti-hepatitis C positive plasma had been enunciated more clearly during the first half of 1990 and following what is now called 'the precautionary principle', the decision to forward anti-hepatitis C positive plasma to the Commonwealth Serum Laboratories was changed. This decision would, even in 2003, be regarded as complying with the highest contemporary international standards of safety.

The Australian Red Cross Society has not received any reports through either the Commonwealth Serum Laboratories, hospitals, medical practitioners or their patients, of acquisition of hepatitis C infection through immunoglobulin, SPPS, NSA or AHF[1] produced from anti-hepatitis C repeat-reactive plasma. To date, the Expert Advisory Group has not been informed of any cases of hepatitis C that can be reasonably ascribed to the transfusion of plasma-derived blood products since February 1990.

Manufactured (fractionated) plasma products from this period have not been implicated in the transmission of hepatitis C. However, in NSW there were a number of cases of transmission of hepatitis C from the use of whole blood or blood components (packed cells, fresh plasma and platelets) in 1990. These cases followed errors in interpretation of complex and confusing technical advice in the introductory phase of hepatitis C testing at one blood collection centre. Some hepatitis C positive plasma from this episode was sent to the Commonwealth Serum Laboratories for manufacture into VIII plasma products. As it was not labelled 'hepatitis C positive', the Commonwealth Serum Laboratories used it as though it were tested, hepatitis C negative plasma. Because this particular problem was first identified in 1992, the Commonwealth Serum Laboratories were not informed of the error until 1992. However, there was a very low viral transmission risk as a result of this incident, due to the known viricidal effects of the immunoglobulin manufacturing process. CSL Limited is not aware of any reports of infection related to this incident. Recall of unused product from these donations by the Therapeutic Goods Administration, Commonwealth Serum

Laboratories with the assistance of the Australian Red Cross followed in 1992.

The Australian Red Cross Blood Service does not say and did not say during 1990 that blood and blood products are free from risk of transmission. It has always drawn attention to the window period, that short period of time between infection and the development of antibody when antibody screening cannot detect infection.

A question HFA is unable to answer is whether the delays in improvement of heat treatment of Prothrombinex (PTX) and lack of ALT testing may have resulted in the transmission of hepatitis which would otherwise not have occurred. HFA continues to seek a full analysis of all reports of the timing of transmissions of hepatitis through haemophilia blood products from TGA, CSL, ARCBS and all governments to ascertain whether any could have been prevented.

The example of the 1992 recall of the CSL product for the treatment of haemophilia B - Prothrombinex (PTX) demonstrates the difficulties for consumers in understanding past decisions and the impact alternative decisions might have had upon their health. Review of questionable bureaucratic processes which are hidden from open and transparent scrutiny cause patients to loose faith in the very systems that are there to protect them. There was a considerable delay before Prothrombinex, heat treated to 80º C, was introduced in mid 1993. This caused frustration and anxiety for clinicians and patients. Some clinicians kept their patients on cryoprecipitate to minimise the risk of larger plasma pools. PTX heat treated to 60º was insufficient to inactivate hepatitis C.

HFA has experienced considerable bureaucratic barriers since May 2003 when it sought information about the1992 recall of PTX. The recall occurred after it was reported that plasma that had not been correctly tested for antibody to hepatitis C might have been used in the manufacture of treatment products. Only PTX was recalled in this situation because the heat treatment to 60ºC was known not to be effective against hepatitis C. The delay in the introduction of the higher heat when it was known that users were not safe from hepatitis C was in itself unacceptable, as was the decision not to recall factor VIII and other products that may also have been manufactured from contaminated plasma on the grounds that viral inactivation processes would not fail. Despite assurances from TGA that CSL stated it had not had any reports of hepatitis C transmission by PTX in the years preceding this incident, HFA is not satisfied that the recall was managed appropriately, whether patients were advised of this recall and that there were no transmissions of hepatitis C resulting from this incident. It is unclear whether any patients were advised of this recall, how much of the product had been used in treatment, and what happened to the product that was not returned to CSL following the recall. Further analysis of this particular incident is required.

It is clear from HFA investigations through discussions and correspondence with CSL, TGA and ARCBS that the recall occurred almost 2 years after the product was distributed and that very little of the product was returned following the recall. Presumably it was indeed used by patients. However, to date, no agency or authority has been able to assure HFA that patients were 1) advised of the recall and 2) whether patients who may have used the affected product were identified and if so, 3) whether they received proper advice and timely testing. This is not known, however some patients would have been tested earlier as the Chiron test became available. HFA now awaits a response from State/Territory Health Ministers as to how each jurisdiction dealt with this issue. The fragmented system at the time, now reported in many documents including the Review of the Australian Blood Banking and Plasma Product Sector (the 2001 Stephen Review), the 2003 report of the Expert Advisory Group on Hepatitis C and Plasma in 1990 (Barraclough Report) and several preceding reports each point to inadequacies in the blood supply system and accountability.

Reliance upon the absence of hepatitis C transmission reports is little comfort in the circumstances, and failure to provide detailed data leads HFA to fear bureaucratic cover up of some sort or an admission that data is so inadequate as to provide meaningful information. Informal discussions with clinicians suggests that many who were in the field at the time do not recall the incident, which would have been quite unusual at the time and therefore of interest, and some acknowledge their records may be scant in regard to these issues, although one would expect testing would have been prudent if patients had been at risk.

There was clearly a view that the Australian blood supply was freer of at risk donors than the USA blood supply which used paid blood donors and was therefore more likely to include donors with at risk behaviours. Further false positives were found to represent 63% of donors in blood bank data in 1990-91 and would undoubtedly have lead people to believe a large number of anti hepatitis C positive donations were not infected with hepatitis C.

Hepatitis C antibody testing was available and used in Australia from February 1990, however donations of plasma which had tested positive to hepatitis C were supplied to CSL for the manufacture of products by the Red Cross until 29 June 1990 when an agreement between ARCS and CSL agreed that antibody positive plasma would not be used in manufactured products. Factor VIII and albumin had been considered to be safe because of their dedicated viral inactivation processes, but there was concern about the impact of removing anti –hepatitis C antibodies from the IVIg and therefore compromise the safety of immunoglobulin. As discussed above, anti- hepatitis C positive plasma was not to be used for Prothrombinex and factor VII, as it was heat-treated to only to 60º at the time which did not inactivate hepatitis C. The debate about the issue in Europe and USA lead to the change in Australia, however Barraclough reports that CSL has not been able to “confirm or deny” whether antibody positive plasma had been used in production processes after June 1990, although internal CSL communications suggest hepatitis C positive donations may have been used in the manufacture of Factor VIII, albumin and immunoglobulins.[21]

By November 1984 CSL was heat treating blood products successfully to eliminate HIV (p45) However, factor VIII which had been heat treated to 80º C for 72 hours was known to inactivate hepatitis B, HIV and NANB hepatitis. The Elstree Blood Products Laboratory in the UK had used this method and there had been no cases of NANB hepatitis found in patients since 1985. [22]Its introduction in Australia was delayed for several years until it was used in 1989 in Australia. Presumably this provided reassurance that the 1990 decisions to use blood that had tested positive for hepatitis C antibodies were acceptable. At the same time however, France introduced hepatitis C testing of blood donations and extended testing to plasma for fractionation.

Barraclough concluded following his investigation of a relatively small period of time in 1990 that “we are also able to conclude with a very high degree of confidence, that those decisions did not result in any user of blood plasma products becoming infected with hepatitis C”. Barraclough went on to say the cardinal principles underlying current concepts of the safety of blood derived therapeutics from infection by pathogenic organisms are:

- The selection of donors from populations at low risk of carrying transfusion transmitted pathogens
- The screening of such donors using appropriate laboratory tests
- The treatment of the products using measures that eliminate any residual risks.[23]

The fact that authorities continued to use donations from those who had tested positive in the manufacture of factor VIII and other products is a risk that HFA believes, even with the benefit of hindsight, is one that should not have been taken.

In Australia there has not always been a timely introduction of new viral inactivation procedures on the grounds that product yield will decrease or the cost is too high. For example, the introduction of the double virally inactivated plasma derived factor VIII product, Biostate in April, 2003, had previously been subjected to considerable delays. Biostate was introduced many years after other countries had introduced such a product with its additional inactivation steps, thus exposing the Australian haemophilia A community to unnecessary risk (see below). Heat treatment of Prothrombinex to 80º C for the treatment of haemophilia B was delayed until 1993 is another example of unacceptable delays.

13. CURRENT TREATMENT PRODUCT SAFETY

Recombinant treatment products have been available in Australia to relatively few people. They were first imported here in 1994 when CSL had been unable to produce sufficient supplies of plasma derived factor VIIII. Recombinant factor VIII has been restricted to children who were not already infected with hepatitis C and/or HIV. In 2001 recombinant factor IX became available and this too was provided only to children who did not have blood borne viruses in all State/Territories except SA where it was not available at all until August 2003.

Government policy means that most people in Australia still must use plasma derived products even though safer alternatives are available and despite the recommendations of the Factor VIII and Factor IX Working Party of the AHMAC Blood and Blood Products Committee. The Working Party last met in November 2000, but its report was only tabled in June 2003. It contains several relevant recommendations affecting safety and quality, the most significant is a recommendation to switch people with haemophilia A and B to recombinant concentrates by 2004. Despite consideration of this issue at each of the July and November Australian Health Ministers' Conference, these recommendations have still not been adopted.

In May 2003 the Expert Advisory Committee on Hepatitis C and Plasma in 1990 (Barraclough) recommended the implementation of the Factor VIII and Factor IX Working Party recommendations following its retrospective review of the impact and risk of hepatitis C transmission through the blood supply.

In March 2003, the intermediate purity CSL plasma derived factor VIII AHF (HP) was removed from the Australian Register of Therapeutic Goods because it was not considered safe enough and was to replaced by Biostate that is a high purity factor VIII with double viral inactivation steps. CSL was later in releasing product than other countries also using this technology because it was having difficulty in achieving desired yields. Astoundingly, all stocks of the soon to be de-registered product were issued by CSL to ARCBS immediately prior to that date and the product continued to be prescribed to patients until the stocks were exhausted. HFA lobbied unsuccessfully to governments and clinicians that this was poor practice and imprudent in view of past experiences and subjected patients to unnecessary risks when an alternative safer plasma derived factor VIII was available, albeit in short supply, and when further supplies of recombinant factor VIII could be purchased to meet clinical need. As anticipated, the yield from the source plasma was lower and CSL has been unable to generate a sufficient supply of this safer blood product. The shortage is not expected to pass until well into 2004. After considerable discussion at State/Territory jurisdictions and the Jurisdictional Blood Committee, agreement was reached in late 2003 so that recombinant factor VIII could be purchased to top up this shortfall. HFA believes that several jurisdictions went to get lengths to avoid the additional cost of recombinant product which each would need to share under the National Blood Agreement, in contrast to using plasma derived product which would be supplied freely under the Plasma Fractionation Agreement. This resulted in unnecessary and unfair anxiety and fear for some patients whose home therapy supply was rationed.

Despite the recommendations of these government agencies and committees, patients continue to be placed at risk by being forced to use plasma derived treatment products which are more likely to expose them to blood borne viruses and agents, known and as yet unknown. The Commonwealth, and State/Territory governments have been considering the recommended switch to recombinant products for several years. Countries with similar health care standards and expectations have accelerated programs to do this in recent years and now Australia falls well below international standards. HFA has lobbied strenuously for this, and is at a loss to know why health ministers fail to accept the advice of their own expert committees and increase the safety of this vulnerable group of patients. The AHMAC Factor VIII and Factor IX Working Party Working Party Report, completed in late 2000, was not tabled until June 2003. HFA fears the recommendations of this Working Party will continue to be ignored, not withstanding further committee work having been initiated. The delays should be of concern to all given the history of litigation and criminal action taken in other countries that failed to provide safe products when they could have done so.

By the early 1980's procedures were in place to inactivate hepatitis. Heat treatment of clotting factor concentrates to inactivate HIV was possible in late 1984 and in 1985 several studies were published to confirm this. Unfortunately if more work had been done to eliminate hepatitis in concentrates, more HIV and hepatitis would have been prevented, but hepatitis was seen as a manageable complication of effective haemophilia treatment. (Krever p757) . In Australia, the dry heat treatment of factor VIII to 80º C that was introduced in 1989, and for factor IX in 1993, has been effective against hepatitis C.

The experience of people with haemophilia through the HIV and hepatitis C epidemics is evidence of their reliance on the safety of the blood pool and their extreme vulnerability to any emerging infectious disease or agent. In each epidemic those in charge of blood collection acted with good faith, even if negligently to try to prevent infections. In each epidemic most people with haemophilia were infected. The assurance that all reasonable steps are being taken to safeguard the blood supply, "based on current knowledge" provides little comfort to people with haemophilia given their experiences. If an alternative safer product can be supplied, it is reasonable and prudent to supply it and the government, doctors, hospitals and other bodies may be exposing themselves to potential claims for negligence if a new illness or infectious agent did emerge.

14. THE NATURAL HISTORY OF HEPATITIS C

Even though the existence of NANB hepatitis has been known for many years little has been known of the natural history of the disease until the last few years. Many people who acquire hepatitis C clear the virus spontaneously and unless re-infected will not develop chronic hepatitis. They will be antibody positive, but RNA negative on PCR testing. Once chronic hepatitis C is established by persisting viraemia, the course of the disease will be highly variable, but protracted. Although there is a clear relationship between chronic hepatitis C and cirrhosis, liver failure and hepato-cellular carcinoma (HCC), there is uncertainty about the rate of progression to advanced liver disease, the proportion of people who will develop these complications, and predictors of disease progression.

Dore estimates that based on current data, 70-80%of people initially infected will appear to progress to chronic infection. [24] Many people have impaired quality of life prior to the development of advanced liver disease, however the major morbidity is associated with progression to cirrhosis and liver failure and/or HCC.

Dore refers to several studies of post transfusion hepatitis C following antibody testing which confirmed NANB hepatitis as the cause of about 90% of prior cases of post transfusion NANB hepatitis. Several studies which have followed disease progression in people with post

transfusion hepatitis for 10 -15 years indicate a cirrhosis prevalence of 10-20%. The Seef study found no greater mortality among people with NANB hepatitis Compared to controls after 18 years of follow up. Dore goes on to note that despite post transfusion hepatitis C appearing to have no effect on survival over the initial 20 years of infection, more than 20% develop cirrhosis over this period and would be at high risk of progression to liver failure and/or HCC over subsequent decades. Studies of two groups of women in Ireland and Germany who were infected with hepatitis C through contaminated immunoglobulin indicate low rates of cirrhosis and in the Irish group 80%of women had little or no fibrosis. It is difficult to know what other factors may have impacted on these findings, such as low virulence of hepatitis C strain, gender, low alcohol use. They were all infected with genotype 1b, which has been associated with more rapid progression. Heavy alcohol intake was linked to those with cirrhosis suggesting that was a major co factor for that sub set. Rodger reported 8% cirrhosis after 24 years of infection. Dore notes there is conflicting evidence about whether mode of transmission and/or dose of hepatitis C is related to disease progression. In some studies of people who have been infected through blood products there is a suggestion of a more rapid progression, however the key issues could be older age at infection or other chronic diseases processes. Dore notes the conflicting evidence about the link between high viral load and progression compared with HIV where viral load and progression are linked to advanced HIV. The role of genotype is also uncertain, however some genotypes are known to have a poorer response to antiviral therapies.[25]

In summary, Dore concluded that the influence of viral load is not fully assessed on disease progression to advance liver disease, but there is strong evidence for genotype, mode of acquisition and gender, and there is strong evidence of the impact of alcohol, stage of fibrosis, age at infection, duration of infection, co-infection with HIV, and/or HBV (p95). The estimated prevalence of cirrhosis among people with chronic hepatitis C is 5 - 10% after 20 years and 15 - 20% after 40 years duration of infection. The risk of HCC, liver failure and death are 2, 5, and 4% respectively.[26]

Dore developed an algorithm for the natural history of hepatitis C. Of 100 people with antibodies to hepatitis C, 20-30% will clear the virus, and 30-40% of the remaining PCR positive group will have consistently normal ALT levels and 60- 70% will have consistently or intermittently abnormal ALT levels and 5- 10% will go on to cirrhosis after 20 years of infection
(3-5% of this group will go on to liver failure and/or cancer) Thus most people with chronic hepatitis C will not progress to advanced liver disease, but may have impaired quality of life.[27]

15. WHAT DO WE KNOW ABOUT PEOPLE WITH HAEMOPHILIA AND HEPATITIS C?

Before the heat treatment of clotting factor concentrates in the mid 1980's almost between 85-90% of people with haemophilia who were exposed to clotting factor concentrate developed NANB hepatitis, which was subsequently identified as hepatitis C. Lee reports that in countries which virally inactivated products, there has been virtually no transmission of hepatitis C since 1996, but it nevertheless remains a high risk factor in countries where single donor, unsterilised preparations such as cryoprecipitate may still be used. [28]Most people who used Australian manufactured concentrates prior to 1990 have been uninfected. There has been no known infection since additional heat treatment of factor VIII concentrates in 1989 and factor IX in 1993.

This exposure to NANB hepatitis with concentrates means that many people in the haemophilia community have a history of more than 20 years of infection and would have received a high viral burden. Many who were young at the time of infection may have cleared the virus, however those who were older at the time of infection and after receiving many doses of infected product may well have a different health outcome. In the questionnaire

completed by many HFA members in late 2003 many people indicated that they are experiencing more problems due to hepatitis C.

It is not known to HFA how many people have progressed to cirrhosis and/or advanced liver disease or who has been diagnosed with HCC, or died from hepatitis C. Anecdotally we have heard of several deaths due to hepatitis C, however this will need to be confirmed with surveillance authorities and AHCDO.

Lee related the results of two studies of people with haemophilia who had received large pool concentrates and infected with hepatitis C. [29] The1994 Tefer et al study found at 20 years duration progression to liver failure was 11%. (p133) However this study was updated in 1999 and it was reported that 30 out of the 305 (10%) had cleared hepatitis C on the basis of repeated PCR testing. Most of these patients however, did not have severe haemophilia and would have been exposed to less frequent clotting factor treatment. Those that cleared were also younger at first exposure and their immune response may have been more effective. At 25 years post exposure 19% progressed to liver disease. Both studies showed that people with HIV and hepatitis C co-infection had an 18 times higher risk of death than those with only hepatitis C (p133). However Lee also noted that there were reports of people with co-infection who cleared hepatitis C nevertheless. The later Tefer study showed that people in the study with hepatitis C only progressed very slowly, with 3% progressing to liver failure and that 76% of those who died were co- infected with HIV. Alcohol use was associated with deaths in people who only had hepatitis C to liver failure (3%). Lee noted that co factors affecting the outcome of hepatitis C are age at infection (younger people have a greater chance of responding to treatment), co-infection with HIV, excessive alcohol use because alcohol increases hepatitis C viraemia, HIV co-infection and genotype. [30]

Lee referred to a study reported in 2001 that involved three centres, the researches concluded there was slow progression of hepatitis C infection in a group of hepatitis C infected people with haemophilia. 14% of the patients with a 15-34 year history of hepatitis C cleared the virus spontaneously. 86% were hepatitis C RNA positive and of these, 69% had non progressive liver disease and 7% had cirrhosis. Lee described an UK 1997 study that showed mortality from liver disease was 16.7 times higher than for the general population, however cumulative risks for those infected with hepatitis C only were relatively lower than those infected with HIV also. However, a Sheffield study showed a high incidence of cirrhosis in people with haemophilia and hepatitis C alone. [31]

16. TREATMENT FOR HEPATITIS

Many people with haemophilia report to HFA that hepatitis C mono - therapy was unsuccessful for them and they fear undergoing combination therapy. This was evident in the HFA 2003 questionnaire respondents who were clearly struggling with the decision or not to undergo treatment. Makris et al in 2001 reported that although interferon was of value in chronic liver disease, sustained remissions were only achieved in 20% of non haemophilia patients after treatment for 12 months. In individuals with haemophilia, the sustained response rate appeared to be even lower due to genotype, high hepatitis C viral load and the presence of cirrhosis. However with combination therapy with alpha - interferon and ribavirin there had been significantly improved responses which he thought promising for people with haemophilia. Makris et al referred to a study by Shields in which 71% of people with haemophilia had remained in remission following combination therapy.[32]

Lee concluded that antiviral treatment is important and that treatment results appear to be similar for people with haemophilia as for the general population, although patients with non genotype 1 respond better to those with type 1, and younger patients without cirrhosis may have improved response rates.[33]

Because little is known about the optimal treatment for people with haemophilia and chronic hepatitis C who were treated with pooled plasma products Schulman et al undertook a study of 61 patients with haemophilia A, haemophilia B and vWD who were undergoing either 6 or 12 months combination therapy. Overall sustained viral response was achieved in 41% (22% in genotype 1 and 80% in other genotypes, including all who were genotype 2 and there was no difference in the treatment duration of 6 or 12 months. The study was stopped sooner than planned because of changed treatment regimens, however the researchers concluded that the efficacy and safety of combination therapy was equal to other populations.[34]

Hepatitis C treatments have a limited success rate of about 40% for people with genotype 1, which is the most common strain of the virus affecting people with haemophilia and they are unpleasant to take with important side effects. About 1 in 10 people have to stop treatment which usually takes a year, because of the side effects. Many are unable to work during treatment.

17. HEPATITIS C AND HIV CO-INFECTION

The clinical management of people with hepatitis C and HIV is difficult and complex. People who are co-infected progress more quickly to liver failure and are often recommended to have anti hepatitis therapy, however this is difficult if they are already having antiviral therapy.[35]

Between 80 -90%of people with HIV and haemophilia will also have hepatitis C.
HIV co-infection has important affects on hepatitis C disease process, including rapid progression to progressive liver disease in some. A 1989 study reported in1999, showed that in people with haemophilia who had hepatitis C, those with HIV co-infection had higher hepatitis C RNA levels and a greater risk of liver failure. Mortality was higher in people with haemophilia and hepatitis C/HIV co-infection than those with only hepatitis C. Hepatitis C genotype 1 has been reported to be more prevalent in people with HIV than those without HIV and shifts in genotype have been reported in people with haemophilia who are co-infected with hepatitis C and HIV as immune deficiency increases. Morbidity and mortality as a result of liver disease is increased in people with HIV/hepatitis C co-infection. The Sabin study in 1997 showed higher mortality in people with haemophilia and HCV/HIV co-infection with hepatitis C genotype 1. [36]

Treatment of hepatitis C in co-infected people is important as there is a higher risk of advanced HIV disease compared to hepatitis C but concerns about toxicity and tolerability of hepatitis C therapy in HIV patients has been a disincentive to therapy. With increased HIV survival, treatment for hepatitis C is increasingly recommended. A number of people who are co-infected with HIV and hepatitis C are now in a situation where HIV treatments have ceased and are in a position to consider antiviral therapy for hepatitis C in an attempt to avoid further liver damage, improve quality of life and extend life expectancy.

18. THE IMPACT OF HEPATITIS C ON THE LIVES OF PEOPLE WITH HAEMOPHILIA AND VWD IN AUSTRALIA

Early results from a recent Queensland study looking at Quality of Life among people living with chronic hepatitis C infection confirm the clinical impression that individuals with HCV experience a variety of symptoms, and that these symptoms are frequently perceived as being of at least moderate intensity. In particular they highlight the potential importance of physical tiredness, irritability, depression, mental tiredness and abdominal pain as symptoms in people living with hepatitis C. A subset of the participants in the study have haemophilia. Preliminary analysis of the data suggests the group with bleeding disorders may have different prevalence and severity of symptoms. This will require further analysis, however it

suggests host factors such as haemophilia influence the impact of chronic hepatitis C on symptom profile and quality of life.[37]

THE HFA SURVEY - 2003

HFA requested members to complete an anonymous survey in late 2003 about the impact of hepatitis C and their bleeding disorder upon their lives. Responses from those who did not have hepatitis C were discarded. Over 250 responses were received from people who identified themselves as having hepatitis C and/or HIV. HFA had sent the survey to everyone on its database, as it does not keep personal health data on its records and therefore has no way of accurately quantifying how many of its members have a bleeding disorder nor how many are infected with blood borne viruses. Assumptions made over the years suggest that each family affected by haemophilia in this country are represented in our database.

The significant response rate highlighted the seriousness of hepatitis C for them and indicated a strong desire for participation in discussion and decision making about it. Furthermore, many respondents identified themselves and/or made personal contact with HFA because they wished to provide further details or add emphasis to some of their concerns. The responses represented a range of views, and many respondents followed up with phone calls, personal approaches and or/letters to disclose their personal experiences with a passion not previously observed by HFA.

In 2000 HFA conducted a Needs Survey of members, and although this only included very general questions about service needs related to hepatitis C and/or HIV, respondents at the time were clearly worried about future impact of blood borne viruses upon their lives, and a fear that they would become ill from chronic liver disease.

The 2003 survey specifically addressed hepatitis C issues and therefore provided an opportunity for members to be more direct if they had been constrained previously. 226 questionnaires were analysed. Issues raised regarding hepatitis C in the 2003 survey were considerably stronger and expressed with greater passion than in the 2000 survey that might be explained by a number of factors, including greater community awareness, evidence of further disease progression and the personal impact of symptoms – health, psychosocial and economic.

Clearly, a factor for many is the inability to distance themselves from an ongoing fear of other viruses entering the blood supply upon which most people are still dependent for their treatment. The ongoing fear of new and as yet unknown viruses and agents adds a dimension which is impossible to overlook as people who have hepatitis C are forced to receive less safe plasma derived haemophilia treatment products because of government policy. In fact, the criterion for access to safer recombinant products in Australia is that a person does not already have a blood borne virus. Further, there remains an overwhelming personal anger about the discrimination experienced because of hepatitis C and/or HIV, particularly as they have become infected through contaminated blood products. For many, there is a strong belief that infections should or could have been prevented, that the blood sector has again betrayed them and most feel aggrieved that the impact of hepatitis C has not been officially recognized, apologized for or compensated in any way.

Because of the chronic nature of haemophilia and the added problems caused by blood borne viruses, many people are unable to separate the effects of each. The 2003 questionnaire confirmed anecdotal reports from our members that the complications of blood borne viruses has increased the burden of chronic illness and in many cases is a greater problem for them than their haemophilia, whilst for others hepatitis C has been put on the “backburner’ as they try to manage the physical, psychosocial and economic consequences of their bleeding disorder.

Overall, however, the responses to the questionnaire painted a picture of three main groups of people – one which held great fears of future morbidity and mortality due to hepatitis C and a second which was already experiencing major effects of hepatitis C upon their health and capacity to live active and fulfilling lives, some of whom had undergone treatment unsuccessfully, and a third, but very much smaller cohort of people who had hepatitis C but who have not experienced any serious symptoms or illness from it and are not bothered at all at the present time and a sub set of people who are most concerned about the impact of their bleeding disorder than hepatitis C. There was a concerning number of people who were unable to indicate the extent of their liver disease, how far their disease had progressed and had little clinical monitoring. This indicates the need for regular testing, education and monitoring.

For many respondents there was great difficulty (and often no point) in separating out the impact of hepatitis C given the already difficult social, economic and emotional impacts associated with having haemophilia. For many people, in particular those with severe haemophilia and those who also have HIV, the hepatitis C was of lesser consequence.

19. WHAT IS THE ECONOMIC IMPACT OF HEPATITIS C?

A significant proportion of respondents indicated they were unable to work without the threat of disruption due to the need for treatment for hepatitis C or treatment of bleeds. There was a high incidence of casual, part time and intermittent work. Many people were concerned about their future financial status in the event of disease progression. People with severe bleeding disorders are more likely to be unable to work, and carers and family members had to give up work to provide care. Many were in receipt of income support, and many reported that partners/spouses needed to work part-time and/or seek other forms of financial assistance such as rent assistance, parenting payments and family tax benefits.

Very few surveys were completed by individuals in high income earning occupations. Those who worked were often in clerical, trades or unskilled positions. This may reflect the difficulty not only in obtaining work continuity, but also in the difficulty in gaining tertiary education.

20. WHAT IS THE LEVEL OF UNDERSTANDING ABOUT HEPATITIS C TREATMENTS AVAILABLE?

It was difficult to assess the level of understanding about hepatitis C from the survey. High numbers of people who are unsure/unaware of their hepatitis C status may indicate the need to provide information about hepatitis C, or it may indicate that people are aware, but that it is not relevant to them in their own particular circumstances. Presumably people with haemophilia have frequent contact with health professionals, and are provided with hepatitis C education opportunities as required. There was a general trend that people needed education and information about treatments.

21. IS THERE A DIFFERENCE BETWEEN PEOPLE WITH HIV/HCV CO-INFECTION?

There was only one co-infected person with haemophilia B, one with Von Willebrand disorder and 22 with Haemophilia A . For this population group, the seriousness of hepatitis C was far outweighed by their HIV status. Most knew they had hepatitis C, but didn't know the current status of their infection. One respondent said life would be different had he not had hepatitis C, but for most, the social and financial consequences could not be separated out from those already encountered as a consequence of their haemophilia and HIV status.

22. MAJOR THEMES OF RESPONDENTS

- side effects of interferon treatment
- uncertainty of treatment outcomes
- uncertainty about disease progression
- inability to access combination treatment
- concern about discrimination, prejudice, and the association with drug abuse
- avoidance of intimacy
- fear of the consequences of disclosing hepatitis C status
- inability to obtain insurance
- social/relationship difficulties
- depression and anxiety
- fatigue is debilitating
- privacy issues, disclosure
- school students with haemophilia and associated conditions encounter difficulty with school based activities and with social interactions

23. COMMENTS OF THE RESPONDENTS

The following list is a fair representation of the range and breadth of the comments made by members when they completed the questionnaire or contacted HFA for further discussion. Comments are verbatim and have not been modified in any way.

24. HEALTH/TREATMENT ISSUES

I took 12 months off work to have treatment, so did my Mum (26 y.o single male)

At times I have had to cut down my workload because of depression)and that causes all sorts of other problems. It becomes a vicious circle in the end – I feel a bit better, so I do more, then I do too much and become depressed again. The worst thing is cannot see any end in sight either *(34 y.o female)*

My doctor said I should have treatment, but I am worried about whether I would cope – they say its pretty bad and I live on my own – besides I am not sure that I could cope with work as well – and I couldn't afford not to work – I already use most of my sick leave and recreation leave on time off because of bleeds

It's the lethargy and fatigue, its hard to cope with and others don't seem to understand – even my family – and the guys at work get fed up with me because I don't pull my weight

I have had treatment twice, but it hasn't worked for me, so I really don't know what to expect in terms of my health in the future, I do worry about getting cancer because I have had hepatitis for so long (72 y.o male)

One of the hardest things is wondering if/when it will flare up

I do worry about how hepatitis C will affect me in another 20 years

I have mild haemophilia, it is well controlled these day. My greatest concern is about the possible impact hepatitis C might have on my liver in the future

Surgery has been delayed and put off. I know it is because of my hepatitis C, but when I ask the doctors they say that's not the problem and that everyone has to wait. In the meantime my knee has got really bad

My husband has died. Hepatitis C and HIV was listed as a contributing factor on the death certificate.

I didn't know until a year ago that I have hepatitis C. It was a shock the way I found out after all these years. I haven't needed treatment for vWD for many years. If I had been tested before, no one has told me, and I would remember that. It is really hard to deal with it, I think of all the times I cleaned up blood spills with my grandchildren, and of my husband and children. When you find something like this at my age it is really hard. I didn't know where to turn. I only used blood products a few times, it is just not fair (62 y.o female with vWD).

I have chosen not to have treatment because it will impact so much on my earning potential and lifestyle. Besides, I would not have enough to live on if I could not work during treatment. I have elected to go this way because my genotype is not the best one for treatment success, but this might be a bad decision in the long run.

I have haemophilia A with inhibitors to factor VIII. I also have hepatitis C and feel very unwell at times. My life is pretty shithouse actually. I live with pain because I have gone without treatment for so long and the hepatitis is flaring up all the time now. I am not a candidate for treatment so the future doesn't look too bright for me (42 y.o male)

25. SOCIAL CONSEQUENCES

My husband and I have a farm, we are about to retire, and we wont have a lot to live on. I am beginning to spend more time at doctors. I had a biopsy recently and found out I have cirrhosis and will need much more monitoring which means lots of travel. In some ways I feel better knowing, but I am resentful that I have to bear all the costs. I shouldn't have to pay. There should be some compensation for this. Our son lives overseas and we would like to visit him. I cant get travel insurance. I haven't been able to look after my aged parents because of the hepatitis C and even my own children have been "over the top" about infection control issues. It was years before my husband would kiss me after we found out I had hepatitis C. (70 y.o.female with vWD)

Fatigue often means I don't go out with my family. They get sick of that, especially my partner, she feels like she is always making excuses for me (49 y.o male)

I never tell anyone that I have hepatitis C. I am only 15 now and I am not sure if it will affect me in the future. I am well now though. (male 15)

I am a lawyer and sometimes have to take time off work because of fatigue and lethargy associated with hepatitis and occasionally end up in hospital at times for haemophilia bleeds. What is the most painful thing for me though is the discrimination I experience because of hepatitis C in personal relationships. After all these years and after so much attention to community education I cannot understand why there remains so little compassion and sensitivity towards people who have hepatitis C issues.

I found that my personal relationships deteriorated as my hepatitis C progressed to cirrhosis. I think this is because I couldn't keep up with people, and they didn't understand the illness. I didn't have the energy for others and they didn't seem to care about me and I was fairly depressed about it. (male 50 y.o).

I haven't told anyone I have hepatitis C. I won't tell anyone. I don't have to and I don't think it is their business. I don't expect it to affect my earning capacity in future.

26. PSYCHOLOGICAL ISSUES

There is a psychological thing happening here – I have developed fears – fear about what the future holds for me, fear about live disease, fear of cancer, fear about what I would do if I don't respond to treatment sometime down the track if I need to have treatment. All this affects me now – its just having to live with knowing you have hepatitis C and knowing the doctors don't really know enough about it still. The counsellor is helpful but it is really hard living with something that could be a time bomb – no-one really knows

Its all about quality of life. Ours is really poor now. I am self employed with a wife and 2 kids – I had two lots of unsuccessful interferon treatment for hepatitis C. Not sure if I can face combination therapy. We had to sell the house because of financial problems because I couldn't work a couple of years ago. I worry that I may not be able to look after my family. Hepatitis C has destroyed my quality of life and now endangers my family. My family has had to endure our decline from a normal lifestyle with security to not knowing what tomorrow will bring and living from day to day. I have the disease, but the others are the ones suffering

Career and employment issues are now secondary thoughts for me. Now I have a two year old son, I am more concerned about how long I will be here for him

This is no fault of mine, but I have to live with this monster, and I do think the government should provide more support and financial assistance to people like me

I have no family. Hepatitis C broke up marriage.

27. DISCRIMINATION

I still feel like an outcast – some of my teachers and friends discriminated against me when I was at school because of my haemophilia and then when my parents were told I had hepatitis some teachers were pretty bad about it - so now I don't tell very many people at work about the hepatitis if I can get away with it, and luckily I am not sick, but they can see my haemophilia (35 y.o male office worker)

I encounter people who think I am lazy. They don't understand fatigue of hepatitis C

My parish priest doesn't want me taking communion

We are discriminated against, probably because hepatitis C is associated with drug use.

I was recently made redundant after being in the same senior position for 13 years. It is great because I recently cleared hepatitis C after having treatment. But when I was undergoing my treatment I told the company CEO and a few others at work. I am still not sure if this was the reason they made my position redundant (55 y.o male)

Health professionals treat me most differently and even the people who do my blood tests often ask me how I got hepatitis C

I don't tell people I have hepatitis C, but then I feel guilty and avoid them.

I am an allied health professional and I don't tell people/colleagues of my hepatitis C status because so many are so judgmental about others with hepatitis C that I don't want them to know I have it.

I live in a small country town. It is really difficult to have any privacy here. Everyone knows your business. I live in fear of the doctors' receptionist telling my neighbor I have hepatitis C. I

go to swimming classes for gentle exercise as I have arthritis and pain from my bleeding and one day the women were all talking about what they would do if someone came to their house with HIV or hepatitis C. I was terrified and I didn't go back. I won't contemplate treatment as I would have to travel so far – it just wouldn't be possible locally (female, 74 with vWD)

I can't get work because of both my haemophilia and hepatitis C. The bleeds and hepatitis C fatigue stop me from working. I lost the last job because I had to take hours off for treatment. It effects relationships also. But I reckon hepatitis is worse than haemophilia because the discrimination is worse. The dentist steers clear of me, leaves me to the last patient and it always looks like he has cleared the room the surgery before I arrive (male 22)

28. RELATIONSHIP ISSUES

For the first few years of my marriage there was constant friction and tension with my wife because of my constant tiredness and sickness (45 y.o male with mild haemophilia and chronic hepatitis C).

It was all I could do to keep up at work – I couldn't do anything around the house, I didn't pull my weight – I let her down in our marriage (54y.o male)

I have no doubt that hepatitis C caused the failure of my first marriage (43 y.o male)

Our sexual relationship has been quite restricted because of the fatigue

I stopped having sex with my partner because I was scared I would give her hepatitis even though doctors told me this would be unlikely – she already had to cope with my haemophilia (49 yo male)

It is a real strain on our marriage. Often I am not well enough to go out and I feel unwell. I can't do my share with the kids. She has to do it all and she is working part time as well (47 y.o male with son 20 at university and daughter 17 at school)

I am 17 and I haven't had a girlfriend yet. Most of the girls I know now know about my haemophilia and they understand I won't die from a cut, but they don't know I have hepatitis C
Hepatitis puts a lot of stress on my family. I only have mild haemophilia and I am pretty much OK most of the time from that point of view because I don't have many bleeds, but I am often too tired to be a dad and do my share. (34 y.o male with 3 children under 12)

It's really hard, I don't let myself get close to people, and I haven't had a girlfriend either. How could I tell her my story – I feel like I have no future, no health, no money, and lots of anger. It's not a good look (25 y.o male)

For years my wife and I couldn't understand why I was coming home tired and exhausted. My wife thought I was rejecting her sexually. I always went to bed early leaving her alone or to deal with the household issues that needed to be taken care of. Often I spent the weekends sleeping just so I could get through the next week. In the early days of our marriage we didn't know why I was like this, but after a few years I was diagnosed with hepatitis C. It all started to make sense after that, but by then we had already distanced from each other emotionally – it has been really hard -

Relationships and marriage are a big problem for people with hepatitis C. The biggest issue for me is that my wife's family is really scared of it and that causes a lot of tension (55 y.o male).

I gave up sex out of consideration for my wife. This hepatitis C is mine, and I have no intention of sharing it (71 y.o male)

29. CAREER LIMITATIONS/RESTRICTIONS

Several male and female medical, nursing and allied health professionals have indicated they have avoided specialties in their disciplines which involve procedural interventions and/or the need for disclosure of their viral status

I am careful about what work I do, and which of my professional colleagues I tell, because I have found health professionals to be the most judgmental about hepatitis C (32y.o female)

It's not the present that makes hepatitis C a problem. It is the potential for the future - it could become a major problem for my work (28 y.o male)

I am only a student, but I am worried that when I have to do shift work in hospitals I won't be able to keep up with my peers because of fatigue. It is already a problem and I am only just a student (20 y.o male)

I am an engineer. I had to cut back my hours and pass up opportunities for promotion because I knew I wouldn't cope with too much stress and long hours of work. It's not my haemophilia that is the problem, it's the hepatitis (59 y.o male)

I have mild haemophilia, but that is not a problem, as I rarely have bleeds any more. Recently I had the choice of 2 jobs – one with a salary of $60,000 p.a and another at $130,000 p.a. The higher paid one fits well with my competence, tertiary education, career goals and interest, however I accepted the lower paid position with less responsibility as I knew I would struggle to manage the additional hours and sophisticated input required as my health is too unreliable these days. My wife and I have decided not to have any children because of the health problems I have because of my hepatitis C, but we have a mortgage and I remain concerned that I will leave her with financial commitments that she cannot meet (36 y.o male)

Hepatitis C influenced my early retirement from my position as a university academic. I needed treatment and had interferon early on. It was not successful and the side effects had affected my confidence so much that I really did not feel able to continue at the level I was previously operating. Now I live with a permanent anxiety that the liver disease will progress.

30. INCOME/ECONOMIC ISSUES/CAREER CHOICES

I have just been told I have cirrhosis and my health has been deteriorating. I work for myself, and expect my income will reduce by 50% this year.

I only have mild haemophilia, but I have a lot of hepatitis C! I am on and off work all the time and will be starting treatment soon. My parents encouraged me to be independent, capable, and ambitious. I manage my haemophilia really well, but I get really angry when I think that it is not my haemophilia that restricts me, but the hepatitis C. Hepatitis C has limited my choices and stopped me going into the career I wanted. I won't have the money for further education after that, so I am not sure what I will do, even if the treatment is successful (22.y.o.male)

My income has decreased over the years. I have had to reduce the amount of work I do – especially while I was waiting to get my knee replacement and even now I still have to take time off because of bleeds, and when my hepatitis C got bad and I started treatment I had

even more time off work because I was tired all the time, and I really suffered from the side effects. My hepatitis didn't clear with treatment so I am back to square one now

I had to find a safe, secure job with flexible work hours so I can take time off if I have bad bleeds or in case I have a hepatitis flare up (32 y.o female with vWD)

Hepatitis C has affected my ability to study and get on in my job. The stress of worrying about it makes it harder. I had to overlook more senior positions because I knew I couldn't cope (44 y.o male)

My son is 17 and still at school. I am worried for his future, and his income potential, whether he will be able to work full time. His haemophilia is fine, he is on prophylaxis and he doesn't have very much joint damage, but I worry most that hepatitis C will interfere with his life. His genotype is the least likely to respond to treatment - what would he do then – he is only 17 – he wants to go to university next year

My income decreased by 40% in 10 years. I had a good career ahead of me, but I decided to leave that and work from home. My wife works so we can keep up our mortgage payments and the kids' school expenses but it's pretty hard on her

I have used all my sick leave with hepatitis C and now when I have to take time off, it has to be unpaid leave

I have reduced my hours to save energy, but I still get really tired and find it hard to keep up with work and have some sort of social life

I would like to see government financial support. What if my hepatitis C takes a turn for the worse? I am self employed with three children and a wife to support. I am self employed and I can't get loss of income or disability insurance because of my haemophilia and hepatitis C (34 y.o with 3 children aged 8, 5 and 3)

I wasn't really well enough to manage a full working week, especially as I would become tired and lethargic in the afternoons, so I negotiated to work reduced hours. This meant a reduced income as well, but I thought I could adjust to that. But the problem is somehow I am expected to do more work in less hours and now I suffer from stress. I am not sure that it is any better, in fact I think it is worse for me now -

I used to be a teacher. My wife can only work part time because she has to help look after me. I am on a pension. Hepatitis C is a greater problem for my health now than my haemophilia 48 y.o male)

I am an experienced IT professional and now find that C has affected my work performance. The tiredness and depression has affected promotion. It's difficult to compete in this day and age when you are not feeling as good as the people you are competing against. They have an immediate advantage over you. (38 y.o male)

I have given up my work in the bank because of hepatitis C

Shift work became impossible for me when I was having treatment because I was tired all the time and could not operate the equipment safety.

We are talking about selling our house and moving to a lower cost area.

I have moderate haemophilia, but that doesn't cause any problems with my work, but because of hepatitis C I have been afraid to take on a higher management position thatg has

been offered to me. I feel it is more important to try and lead a stress-free life and manage my health and well being carefully (male 44)

Uncertainty about my health is the reason I didn't pursue career advancement and seek higher paid positions. I have had treatment for hepatitis C but it was not successful so I am not sure what my future will be. I didn't finish my university studies, and now that I look back on it and don't like to admit failure I know it was because I just wasn't well enough to do all the work. I couldn't concentrate and I was sick fairly often and I became depressed at one time

THE NEED FOR FINANCIAL ASSISTANCE

31. HISTORY OF FINANCIAL SUPPORT FOR PEOPLE WITH HIV

More than 250 people with haemophilia were infected with HIV through their treatment with contaminated blood clotting concentrates prior to the introduction of viral inactivation procedures in 1984. In 1989, the Federal Government accepted the principle of providing financial support for those infected, establishing the Mark Fitzpatrick Trust. Payments from the Trust have been a combination of lump sum and regular payments. Subsequently, between 1991 and 1994 all State Governments provided financial assistance packages to people with haemophilia and HIV. Governments established the Mark Fitzpatrick Trust, and made State settlements not on the basis of accepting legal responsibility, but rather as a "moral responsibility" to provide financial help to those infected with HIV through products provided as part of their health treatment. Those eligible received an initial payment, and subsequent annual payments determined upon the level of severity of physical impairment. Claims could only be made if infection transmission occurred before May 1985. Payments were made to 425 beneficiaries. The Trust was wound up in 2001 when the remaining funds were distributed.

When the trust wound up, many people were healthy and had lived longer than expected when the Trust had been established. Many continued to experience financial hardship. The issues for people who are co-infected with hepatitis C are complex, and at the time the Trust was established the health problems of this group of people who also had liver disease was not anticipated (see below under co-infection).

Those who believed they could prove a case of negligence took separate legal action against blood transfusion services, CSL, hospitals and clinicians. Court action focussed on delays of transfusion services to acknowledge the risk of AIDS through blood products, the failure to implement donor declarations to exclude at risk donations, delay in introduction of surrogate testing, delay in heat treatment of products etc. Many people could not identify when they had become infected and thus it would be difficult to be successful. HFA lobbied further for compensation rather than the need for establishing negligence and threatening relationships with treaters, and discrimination by the health system. The successful PQ case against a hospital succeeded on the grounds that the patient should have been informed of the risks of factor VIII concentrate in September 1984 when treatment was changed from cryoprecipitate

to AHF. After huge costs of litigation in this and another case, State governments (except NSW) agreed upon out of court settlements with governments with payments ranging from $100000 - $650000. In NSW people with haemophilia refused to sign away rights to sue when amounts up to only $50000 were offered by way of a settlement offer. [38]

32. FINANCIAL SUPPORT FOR PEOPLE WITH HEPATITIS

People with haemophilia infected with hepatitis C were infected in the same way as those who became infected with HIV through contaminated blood products given as part of their health treatment prior to 1989. No financial help has been made available to the people infected with hepatitis C who are not co-infected with HIV. There is clearly a great need for this. For people with haemophilia, the added health and psychosocial consequences of hepatitis C upon an already potentially debilitating chronic disorder warrants special consideration.

33. MORAL RESPONSIBILITY

The many recent personal stories related to HFA for the purposes of this submission have highlighted the increasing concern for the community about hepatitis C. Many people feel betrayed by the blood system they had been encouraged by the authorities to trust. They had no choice but to use the products which caused them harm, and even death.

Haemophilia is a significant life challenge in itself, however the complication of hepatitis C illness and progression of liver disease with increasing years of infection, leads many to fear and anxiety about their future health and treatment needs, and creates doubts for the security of their social and economic future, and that of their family and loved ones.

That the hepatitis C infection has occurred through the blood supply leads to a greater sense of betrayal – first HIV and now hepatitis C,and …….what next? The haemophilia speaks openly and with strong feeling about TNV, The Next Virus. For people with haemophilia there is the ongoing fear that unknown viruses and agents such as vCJD could slip through the blood supply. As new experiences of blood borne viruses and infections occur the fears are exacerbated. The theoretical risk of transmission of vCJD through the blood supply was realised in December 2003 when a person in the United Kingdom who had received a blood transfusion from someone who had later developed vCJD, also developed vCJD. New, and as yet unknown viruses are likely because of the time lags between when new viruses are identified and when testing methods are developed and implemented.

People with haemophilia who live with the consequences of contaminated blood products are supported by competent virologists, immunologists, blood transfusionists and regulatory officials who share their concerns about the possibility that a virus or agent is a real risk, hence their advocacy for risk reduction strategies.

Concerns about blood supply safety in the media suggests many people in the broader community are also worried about the blood supply, and how decisions have been made in the past and now, but for the haemophilia community which must live with the consequences of the past and hold real fears for the future, it is even more difficult.

Many feel they have been betrayed by the blood system in the past and feel this even more so now because they are forced to use plasma derived haemophilia treatment products, even when safer alternatives are available, because of direct government policy not to provide them. It is a further insult that the main criterion for rationing these safer recombinant treatment products in Australia is blood borne viral status and age.

34. THE CASE FOR FINANCIAL ASSISTANCE

"The compassion of a society can be judged by the measures it takes to reduce the impact of tragedy on its members. Although the risks to the users of blood components and blood products today may be low, serious disease and some deaths will continue to occur as a result of the therapeutic use of blood.

There is, moreover, always the likelihood that a new and mysterious blood-borne pathogen may strike. …. it is of little consolation or even relevance to those unfortunate members of our society who suffer from infection caused by blood transfusions or blood products that the blood supply now is adjudged relatively safe. A system that knows that these consequences will occur and what brings them about has, at the very least, a moral obligation to give some thought to the question of appropriate relief for those affected by the inevitable events".

Krever Ch 39

The legal grounds of negligence upon which settlements have been made for many people with medically acquired hepatitis C are not applicable to the majority of people with haemophilia.

People receiving a blood transfusion had a single medical episode, and exposure to the blood of less than five people. It can be dated and traced back to specific donors. People with haemophilia were, and continue to be exposed, to the blood of tens of thousands of people, often twice per week. We now know that before blood products were treated sufficiently that all people with haemophilia who used those concentrates between 1985 and 1990 were being infected and re-infected.

People with haemophilia were infected at the same time as those who received blood transfusions. In fact, the risk for infection is increased for people with haemophilia because of the huge number of donors they are exposed to. It is unfair that those who were infected with hepatitis C from large pools have no redress when they were in fact at greater risk. The requirement of proof that a donation caused an infection is flawed. Common sense dictates that people with haemophilia became infected in the same way as those who did so through a blood transfusion.

The full impact of hepatitis C as well as haemophilia on people's lives is very hard to appreciate. Apart from the various physical symptoms experienced, there is also the extreme anxiety of living with multiple health issues, each of which is potentially life threatening.

People with haemophilia infected with hepatitis C were infected in the same way as those who were infected with HIV and those problems were recognised. On "moral grounds" they should, therefore, be similarly offered financial help. Government has already recognised the moral case for financial assistance for those infected with HIV. Haemophilia Foundation Australia would like to see the principle extended to those infected with hepatitis C on grounds of equity and social justice.

35. THE FINANCIAL NEED

Financial support would at least help alleviate some monetary stress for infected people. Financial support is essential to enable this group of people to deal with the day to day and long term consequences of hepatitis C obtained through the blood supply through no fault of

their own. Payments could be used both to target specific identified needs as well as to provide resources to allow infected individuals to regain some control over their lives. In the absence of a cure or a preventative vaccine for hepatitis C, education and prevention strategies remain the most important mechanism for controlling the disease in the Australian community. Different forms of payment could be used to meet the complex and changing needs of those infected.

HFA considers that each person with haemophilia infected with hepatitis C should receive a single payment in acknowledgement of the medical, social and economic impact on his or her lives. All healthcare and medical treatment should be provided free of charge to all people infected with hepatitis C. Further payments should be made available if and when each person progresses in hepatitis C illness, to assist with meeting the additional costs and to ensure financial assistance to relatives who provide care, or suffer hardship because of the disease.

In many other countries just as in Australia government financial assistance for blood-transmitted disease was initially restricted to people with HIV or AIDS. However, because of the high loss of life through HIV there are now more people who are actually affected through blood with hepatitis C than HIV and many of these people experience poor health outcomes and suffer financial hardships through loss of income and high health care costs as a result. Some countries have taken steps to redress this anomaly.

At the XXVI General Assembly of the World Federation of Hemophilia in Seville, Spain, on May 24, 2002 the 77 National Member Organisations present, including Haemophilia Foundation Australia, unanimously agreed on the following resolution:

"The WFH recognizes the pain and suffering caused to people with hemophilia and related bleeding disorders by iatrogenic infection with the hepatitis C virus. The WFH calls on all governments to make available suitable recompense to all those infected and their families

The Krever Commission recommended the Canadian Compensation schemes which has become a model for other countries as they have taken steps to acknowledge and attempt to compensate for the losses associated with hepatitis C. Krever recommended compensation instead of actions for negligence because of the difficulties in establishing fault of an individual or organisation in the case of hepatitis C. Common law is not an effective remedy for many who are injured through no fault of their own. It involves drawn out legal argument in an adversarial environment, high costs of litigation and unpredictable outcomes, none of which is helpful if you are sick, or already financially disadvantaged because of chronic illness, undergoing toxic antiviral treatment and/or necessarily forced into litigation against the same people who continue to provide your treatment – as was the case for many people with haemophilia with HIV litigation and would be the case for individuals now if they mounted action in respect of their hepatitis C infection.

The significance of hepatitis was disputed until the HIV era, therefore the production of virally inactivated concentrates was a low priority until 1984/85.The failure of litigation on the basis of “current knowledge at a point in time” remains a frustration for people with haemophilia who have been affected by contaminated blood products when they had no alternative but to rely on clinicians, researchers, policy makers and regulators to ensure the blood supply and therefore their treatments safe.

Hepatitis C is not unlike the HIV experience for many people with haemophilia. Most people with haemophilia have hepatitis C. More than one person in each family affected by haemophilia is likely to be affected by hepatitis C and/or HIV. The risk of NANB hepatitis has been known since the 1970's. The possible delays in the introduction of screening tests or viral inactivation procedures may have infected more people unnecessarily. People with haemophilia have an increased viral load, often more than one genotype, and a high proportion are known to develop liver disease. There is no way to compensate for the loss of a life or a life of a loved one, but surely there is evidence for a financial assistance package in recognition of the community's moral responsibility to people with haemophilia who have been infected by hepatitis C through the blood supply.

There are various precedents around the world for compensation and financial assistance for people who have been infected by hepatitis C through the blood supply, and in some cases, for their families. Each situation is slightly different in respect of blood safety record and standards, viral inactivation technologies adopted, time/date restrictions, burden of proof and /or the need to establish fault, eligibility criteria, and type of assistance provided and for whom.

The Australian situation may well be unique in some respects, and share similarities with other jurisdictions in other respects, however for people with haemophilia, the background is the same, the pain and suffering is the same and the special needs of this group of people are the same. The effect of hepatitis C on people with haemophilia is significant and perhaps quite different from others who became infected through other modes of transmission. HFA makes no judgement about the validity of other claims for or against compensation or financial assistance, but seeks the acknowledgement of the Senate Committee that the special circumstances of the haemophilia community justifies the provision of a financial assistance package to ease their difficulties.

Further, HFA seeks the Senate Committee's support for a range of other recommendations to help overcome or manage some of the disadvantages affecting the part of the haemophilia community which is so adversely people affected by hepatitis C.

We seek an outcome that reflects a greater sense of justice having been afforded to people with haemophilia, rather than revenge for the failure of individuals or the blood supply system to make them safe. We seek recommendations that strengthen the blood sector in Australia and that optimises the safety and supply of haemophilia treatment products.

HFA supports the principle of self sufficiency, in general terms, as it relates to blood products, however, it must be ensured that sufficiency of required treatment products for any indication is not compromised at the expense of national self sufficiency. It is recommended that Australia adopts systems which allow it to meet the treatment of people who require plasma products and blood components made from blood given freely by Australians. We recognise this is a proud tradition and one that is valued by most sectors of the community, including governments. However, such a principle must never be allowed to continue for political and/or financial reasons and decisions must be based upon evidence, solid data and a sound regulatory framework. A principle of national self sufficiency in this country for some blood products should not be adopted at the expense of best practice for the treatment of haemophilia in this country. Australia needs to retain the capacity to manufacture high quality, well regulated, blood products required by the Australian community to the highest degree of safety possible as well as fund the importation of the safest, gold standard treatment products which, in the case of haemophilia products, are currently those made from synthetic, recombinant technologies in Europe and USA. Policy decisions should be made on the grounds of clinical best practice and safety rather than political, economic and commercial

considerations. There are several examples in the history of haemophilia treatment products in this country where the latter principles have been adopted at the expense of the former, some of which have been mentioned above. This is not acceptable. A policy of self sufficiency must not come at the expense of best practice. All policies should be based upon evidence based medicine, a strong regulatory framework, robust haemo-vigilance and pharmaco-vigilance programs. Guidelines for the clinical use of products should be confined to clinical recommendations rather than non clinical matters such as supply or financial considerations. Furthermore, there should be a clear delineation between policy and the commercial interests of stakeholders which could impact on decision making relating to the clinical use of the products which are the subject of the Plasma Fractionation Agreement.

36. OTHER COMPENSATION SCHEMES/ INTERNATIONAL EXPERIENCE[39]

CANADA

Approximately 1400 people with haemophilia were hepatitis C positive. The Krever Commission recommended compensation for all those who were infected with hepatitis C via blood or blood products. In Canada like in Australia, most people became infected through use of blood products before 1989. Surrogate testing for NANB hepatitis was rejected by the authorities in 1977 and heat treated products were rejected in 1982. In 1986, Canadian authorities refused to introduce hepatitis C antibody testing and opted for a study instead in which half the subjects received screened blood and the other half unscreened blood to find out the efficacy of the test. In 1998 compensation was awarded to all those infected between 1 January 1986 and 1 July 1990 irrespective of the status of their health. The scheme also includes secondarily infected family members or partners. Compensation was also awarded to the partners of those infected, and to dependents of those who had died. The total cost of this program to the government was $1,118,000,000 Canadian dollars plus interest derived after April1998. [40]

<u>The Payment Schedule</u>

First payment if hepatitis C antibody positive	$10,000	(AUD$9900)
Second payment if PCR positive	$20,000	(AUD$19800)
Third payment with fibrosis or needing interferon therapy	$30,000	(AUD$29700)
Fourth payment for cirrhosis	$65,000	(AUD$64350)
Fifth payment for liver decompensation/HCC or after a liver transplant	$100,000	(AUD$99000)

Those who had previously received HIV compensation received a one off payment of $50,000 only (AUD$49500).

Additional payments under the Settlement Agreement are made for:

- monthly payments of $1000 are made for people undergoing treatment in recognition of the strains involved with hepatitis C therapy. The third payment can be waived in favour of a loss of earnings payment and payment for students under the age of 18.
- payments may be made for treatment and medication not covered by insurance schemes in public and private health insurance plans
- compensation is paid for costs of care up to CAN$50,000 per year (AUD$49500)
- compensation for out of pocket expenses related to seeking medical advice, treatment as well as medical expenses for a claim, including travel, accommodation, meals and telephone etc

- compensation for people with HIV/Hepatitis C co-infection
- compensation for deceased persons' relatives, if person died after 1 January 1999, in which case they will receive all payments to which that person would have been entitled for the period up to his death. If person died before 1January1999 the survivor will receive between CAN$50000 - $120000 (AUD$49500 - $118000)
- up to $5000 will be paid for funeral expenses (AUD$4950).
- compensation for dependents and family members for loss of support, loss of services, loss of guidance, care and companionship

UNITED KINGDOM

Approximately 4800 people with haemophilia infected with hepatitis C, representing 47% of haemophilia community. The UK Haemophilia Society has been campaigning since 1995 for compensation on the grounds that hepatitis C is similar to HIV, which has been compensated for by the government, and that there were moral grounds for granting compensation for hepatitis C as well. Between 1996 and 1998 different governments refused to provide compensation.

In 1999, when it became known that non virally inactivated treatment products had been used in Scotland until 1987, a separate inquiry was launched in Scotland. In 2002 the Scottish House of Parliament granted compensation of a minimum of GBP 50,000 . (AUD$119000)

The UK Haemophilia Society's 2002 proposal to government for a scheme based on the Canadian scheme, sought average payments of GBP140,000 per person (AUD$333200) The proposed scheme would pay according to the stage of liver disease reached to allow for individual circumstances and made provision for additional payments for dependents and family, inconvenience of long term therapy, out of pocket expenses and costs of care. It also took into account loss of earnings using research findings demonstrating the financial impact of hepatitis C infection.

Payment level 1	Antibody positive, PCR negative	GBP7500
Payment level 2	Antibody positive, PCR positive	10000
Payment level 3	Fibrosis or having drug therapy	20000
Payment level 4	Cirrhosis (proof may be other than liver biopsy)	40000
Payment level 5	Decompensated liver disease or liver cancer	60000
	(AUD$333200)	GBP 137500

In August 2003 the UK government made an unexpected decision in 2003 to grant a compensation package for the UK.

In January 2004 the UK Health Secretary John Reid announced a scheme that makes people who were infected with hepatitis C from NHS blood or blood products eligible to receive ex-gratia payments from the Department of Health.

"I'm pleased to be able to announce the details of this scheme today. I felt it was important that English Hepatitis C patients should receive these payments on compassionate grounds. It's clear that providing assistance is the right thing to do"

UK Health Secretary John Reid January 2004

Everyone whose hepatitis C is attributable to NHS treatment with blood or blood products before September 1991 will be eligible for the payments (including those who have cleared hepatitis C). The ex-gratia payment scheme means that people infected with Hepatitis C will receive initial lump sum payments of GBP20,000 (AUD$47600) and those developing more advanced stages of the illness - such as cirrhosis or liver cancer - will get a further GBP25,000 (AUD$59500) and people who contracted hepatitis C through someone infected with the disease will also qualify for payment. People with HIV will also be eligible if they have hepatitis C, however the surviving relatives of those who have died from hepatitis C are excluded. The ex-gratia payments will not affect social security entitlements. The payments are considerably less per person than the proposal of the UK Haemophilia Society and time will tell whether this is accepted by the UK haemophilia community.

IRELAND

The Irish Haemophilia Society (IHS) has been involved in many years of negotiations for financial support for people infected with hepatitis C through blood products, including many women who had been infected by hepatitis C through immunoglobulin- Anti D.

In 1994 IHS asked for free medical treatment for people with hepatitis C and in 1995 commenced discussions for compensation for hepatitis C. In 1996, the Hepatitis C Compensation Tribunal was set up and claims were dealt with on a case by case basis. Applicants had to prove on the balance of probabilities that the infection was caused by blood or blood components. Applicants had to agree not to initiate civil action. (Krever Ch).

This scheme was legislated for in 1997. Free medical care <u>for any condition</u> for any person who had been infected with hepatitis C through blood and blood products was also provided for in the Health Amendment Act in 1996. A lump sum was paid in stages to take into account disease progression which may have occurred. Claims from 240 people have been heard, including people with haemophilia, their partners and relatives of those who have died. Payments have ranged from 50,000 Euro to 2.5 million Euro. (AUD$81,500 - $4,077,900)

The payments for hepatitis C infection are made in accordance with the following categories;

- General Damages – pain and suffering, diminished quality of life, the need to be on treatment, higher viral load in people with haemophilia, multiple genotypes and the underlying effects of haemophilia are considered under this category.
- Health Care Costs – covered under the Health Amendment Act (1996)
- Loss of earnings – different test for children and adults, includes actual loss of earning and superannuation entitlements, loss of earning through loss of opportunity. Payments can be tailored to the individual needs of applicants.

In 2003 the Hepatitis C legislation was amended to include people infected with HIV. This was in addition to the payments made under the 1991 HIV compensation scheme where the payments ranged from 100,000 – 130,000 Euro (AUD$163000-$21900). This new scheme covers general damages, healthcare costs and loss of earnings (paid retrospectively with interest at an annual rate of 8%) and the following new areas:

- Loss of consortium (in the case of relationships for 3 years or more, impairment of sexual relations, fear of transmission of hepatitis C, loss of love care and attention due to a spouse being unwell, fatigued or incapable of undertaking normal social activities, loss of ability to communicate, aggressive behaviour would be included under this category).
- Loss of society
- Post traumatic stress Disorder for survivors and dependents
- Solatium – 28,000 Euro (AUD$45700) paid to next of kin and those who died (AUD$45700)

ITALY

In Italy, as early as 1992 the government provided a government funded program of financial assistance for people with haemophilia and HIV/AIDS and legislation was amended to cover people who suffered irreversible liver damage from hepatitis A, B and C. Whilst this program was not without its problems it set up 8 categories of entitlement based upon the severity of damage etc. The amount paid varied up to CAN$43850. (AUD$43425)

NEW ZEALAND

In New Zealand 70% of people with haemophilia were estimated to have been infected with hepatitis C. Most infections are believed to have occurred before 1989. The hepatitis C antibody test was not introduced until July 1992, far later than many other countries, and it is understood that unscreened blood products were used after this date. Under the Accident Compensation Act (1982) HIV had been recognised as an accident due to medical misadventure. Hepatitis C was also recognised as a medical misadventure so that claims could be made, however, the deadline for making claims was sudden and many of those affected missed this. Hence some people were compensated with a lump sum of up to NZ$27000, plus health costs, which were not covered by the government medical insurance scheme. The legislation was amended in 1992 and required an applicant to establish a physical injury resulting from medical error or medical mishap rather than misadventure. A medical mishap is defined as a rare and severe adverse consequence of treatment provided by a health professional, resulting in significant disability. The amendments made hepatitis C claims under this legislation unfeasible which has resulted in much anguish for people with haemophilia who have been treated quite differently in relation to compensation for hepatitis C. (AUD$23700)

37. GOVERNMENT INQUIRIES

There have been several inquiries into hepatitis C transmission, the most notable being the Krever Commission in Canada that after a comprehensive review resulted in compensation for people with haemophilia and hepatitis C. In Ireland there has been two inquiries – the first, the 1996 Finlay Inquiry did not deal adequately with the issues of people with haemophilia, and after IHS negotiations it was followed by the Lindsay inquiry of 2000-2001 which lead to the establishment of the National Haemophilia Council and a product Selection and Monitoring Advisory Group with IHS representation. This gives people with haemophilia a statutory authority right to decision making about their treatment products and services and allocation of funding resources in the future.

38. A PROPOSAL FOR RECOMPENSE FOR PEOPLE WITH HAEMOPHILIA AND vWD IN AUSTRALIA

AN APPROPRIATE MODEL INCLUDES:

- Recognition and apology that contaminated blood caused infections
- No fault financial recompense for all people with haemophilia and vWD who have hepatitis C
- Full and unhindered access to free hepatitis C treatment irrespective of genotype and previous treatment outcome
- Full and free access to all medical treatment for any condition
- Recompense as well as government income support for people whilst having treatment for hepatitis C
- Education on treatment and services available for people with hepatitis C
- Access to free and comprehensive education to alternative therapy and complementary medicine
- Adequate resources for haemophilia treatment centres and co-ordinated access to hepatology and liver clinics to care for people with bleeding disorders
- Comprehensive health care for people with haemophilia who have hepatitis C and /or HIV
- Coordinated, national standards for delivery of hepatitis C services
- Full access to liver transplantation program
- Strengthened bleeding disorder data collection and analysis
- Access to recombinant products for all people with haemophilia immediately
- HFA participation in decision making about the selection of haemophilia treatment products and resource allocation
- Prophylaxis for the treatment of haemophilia in children and adults
- Adequate supplies of the safest treatments for vWD

39. COST OF FINANCIAL ASSISTANCE

In the UK proposal a computer model which simulated the progress of hepatitis C was used to predict the number at different levels of severity of hepatitis C over 10 years into the future. The UK model proposes payment determined by the level of injury at the time the compensation is determined, compared to the Canadian system which stages the payment. In the UK system the compensated person can return for a further payment if they move onto another level taking into account the previous payment. The UK computer modelling is used below as a basis to estimate costs of a similar scheme in Australia the following costs are suggested. It is important that full actuarial calculations on the basis of expected disease progression are made for the Australian situation, taking into account a range of local factors including healthcare costs, common law payment history etc, and that future dollar values are factored into the progressive payments proposed.

On the basis of the estimated number of people with haemophilia, vWD and hepatitis C described above we assume there are approximately 1022 people with hepatitis C.

Payment level		Hypothetical number at 1 Jan 2000	Payment amount per person AUD$	Total payments for level AUD$
1	AB+, PCR-	153	18000	2,754,000
2	AB+,PCR+	130	24000	3,120,000
3	Fibrosis, drug therapy	565	47800	27,007,000
4	cirrhosis	129	95500	12,319,500
5	Advanced liver disease/HCC, transplant	42	143300	6,018,600
Total		1022	328600	51,219,100

The Australian model assumes free and comprehensive medical care irrespective of condition. That is everyone with haemophilia and hepatitis C will be eligible for free health care throughout their life. Further costs should be factored in for additional expenses, such as care, HIV in addition, out of pocket expenses, those who died before the payments were available, dependents and family members.

This model will only be successful if it is supported by strong hepatitis C health, medical and counselling services that are provided to all people with haemophilia and vWD who have been infected with hepatitis C and relevant financial and other support services for their families and carers.

4 February 2004

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[1] UKHCDO in Haemophilia(2003), 9, 1, pp1-23
[2] Ponce, M in Haemophilia (2000), 6, Supplement, 2, 35-52 at p 52
[3] Leslie, D.E et al. (1992) Medical Journal of Australia 156:789-792
[4] HFA has made a best guess estimate based upon unconfirmed data from Australian Bleeding Disorders Registry and data provided by DHA to Senate Community Affairs Legislation Committee, Question EO3-130, June 2003.
[5] Krever at p1048
[6] Report of Krever Commission at p687
[7] Report of the Expert Advisory Group on Hepatitis C and Plasma in 1990 (2003) Referred to elsewhere in this submission as the Barraclough Report, at p61
[8]Wood, Boyce et al in Hepatitis C- An Australian Perspective (Crofts,Dore,Locarnini - Eds) at p249.
[9] Krever at p632
[10] Krever at p696
[11] Krever at p696
[12] Krever at p647 and Barraclough at p41
[13] Krever at p646
[14] Krever at p707
[15] Barraclough at p40
[16] Barraclough at p40
[17] Wood,Coghlan and Boyce in Crofts et al (eds) 2001 at p248
[18] Krever at p695
[19] Wood, Coghlan and Boyce (2001) at p246ff

[20] Barraclough Report (2003) at p 1-4
[21] Barraclough Report (2003) at p12
[22] Barraclough Report(2003) at p78
[23] Barraclough Report (2003) at p81
[24] Dore, G in The natural history of hepatitis C virus infection in Crofts et al (eds) 2001, at p83
[25] Dore, G (2001) at pp 89-96
[26] Dore, G (2001) at p96
[27] Dore, G (2001) at p96
[28] Lee in Haemophilia (2000), 6, Suppl, 133-137.
[29] Lee, C (2000) at p133
[30] Lee, C (2000) at p135
[31] Lee,C (2000) at p323
[32] Makris, Dusheiko et al, Haemophilia (2001),7, 339-345 at p340
[33] Lee, C at p325
[34] Schulman et al, (2002) Haemophilia, 8,129-135
[35] Makris et al, (2001) p 341
[36] Mijch, A in Crofts et al (eds) (2001) at 117-125
[37] MacDonald,G, Uni of Queensland, informal discussions with HFA 2003
[38] Material from several HFA documents and from Sendziuk,P Learning to Trust - Australia's responses to AIDS (2003)
[39] HFA has drawn material from several sources in this section including UK Haemophilia Society publications, Brian O'Mahony , President, World Federation of Hemophilia, report of the Krever Commission, and the 2000 World Federation of Hemophilia Report (Status of Financial Assistance for HCV Infected Persons with Haemophilia in WFH Countries, Update Spring 2000)
[40] The full text of the Agreement can be downloaded from the website www.hepc8690.com