

Service Specifications for Haemophilia and Related Bleeding Disorders in New Zealand

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1. *Executive Summary*

Haemophilia is a complex lifelong bleeding disorder with the potential to cause pain, chronic disability and premature death. It is an inherited disorder with medical, psychosocial and reproductive consequences for multiple family members, male and female, spread over many generations.

A proportion of people living with haemophilia have also been infected with hepatitis C and/or HIV as a result of past treatments.

Children, women of childbearing age and older people affected by haemophilia face specific challenges and require appropriate health care support.

Haemophilia is uncommon, affecting approximately 400 New Zealanders at the present time. Treatment, accompanied by good management, of haemophilia is effective in preventing and treating acute bleeding and reducing long-term joint and muscle damage. It is also highly specialised and very expensive.

A high level of patient and family participation is required for effective treatment delivery. Treatments for haemophilia are expected to undergo major changes due to technical advances in the near future.

It is essential that the use of health care resources is evidence-based wherever possible, and subject to quality assurance including audit.

Comprehensive care, delivered by multidisciplinary teams in a specialist haemophilia treatment centres is the internationally accepted model of care for haemophilia and related disorders and has proven benefits in terms of health outcomes and cost savings.

A national approach to care is required to facilitate the implementation of current best practice, procurement, the effective introduction of new therapeutic products in an equitable manner and to manage high cost interventions.

People affected by other inherited bleeding disorders including von Willebrand's disease, platelet function disorders and the rarer coagulation factor deficiencies have many problems in common with haemophilia sufferers. Health services provided for haemophilia care are well placed to provide appropriate specialist care for people with other inherited bleeding disorders.

This document sets out recommended standards of care for patients with haemophilia and related disorders in New Zealand. It forms the basis for the development of a national service framework for inherited bleeding disorders.

2. *Introduction*

This specification has multiple purposes. The aims are:

- To demonstrate a minimum standard of treatment acceptable to the New Zealand Haemophilia Treaters Group (NZHTG) and the National Haemophilia Management Group (NHMG).
- To inform those with responsibility for commissioning haemophilia services of the service standards that are appropriate for the diagnosis, treatment and on-going care of people with inherited bleeding disorders and their families.

- To demonstrate that although the delivery of haemophilia care is expensive, the lives of patients and their families can be transformed by an adequate standard and volume of care, based on early and preventive prophylaxis treatment in childhood to give a normal life expectancy and to prevent joint damage consequent orthopaedic intervention later in life.

These service specifications have been developed by the NZHTG, the medical advisory group to the NHMG, in consultation with the patients' group the Haemophilia Foundation of New Zealand (HFNZ), and in consultation with Māori. The membership of the NZHTG is shown in appendix 1. Wherever possible, recommendations are linked to formal levels of published evidence (appendix 2).

Clinical guidelines outlining treatment recommendations for individuals with bleeding disorders are produced by the NZHTG. This service specification should be considered in tandem with treatment protocols produced by NZHTG.

3. *Service Objectives*

The aims of the national haemophilia service specification are:

1. To identify and respond to the complexity and rarity of haemophilia and related conditions by establishing appropriate multidisciplinary health care systems for their management, based on the international comprehensive care programme for haemophilia.
2. To deliver care in a way that limits bleeding episodes, minimises pain, incapacity and disability characteristics of haemophilia and related conditions.
3. To ensure that haemophilia care is as safe as possible, complies with national health guidelines, conforms to accepted international standards and published clinical guidelines for haemophilia care and is monitored by appropriate audit.
4. To encourage the development of a holistic approach to patient care, assuring that all patients have access to specialist multidisciplinary services.
5. To be responsive to the lifelong medical and psychosocial needs of patients and their families.
6. To encourage an environment in which patients are able to make informed decisions about treatment.
7. To promote the delivery of haemophilia care within the setting of the patient's own community involving primary, secondary and tertiary care services where possible.
8. To enable people with inherited bleeding disorders to optimise their quality of life and maximise their potential as active and productive members of their communities.

4. *Target disease and patient groups*

The conditions covered by the service specification are:

Condition	ICD10 code
Congenital haemophilia A	D66
Congenital haemophilia B	D67
Female carriers of haemophilia A and B	
Congenital von Willebrand's disease	D68
Rarer congenital coagulation defects	D68 -1 and D68 -2a to i
Inherited platelet disorders	D69 – 1a to e

The target patient group includes children and adults with bleeding disorders and asymptomatic carriers of the genetic mutations responsible for these disorders.

Foreign visitors without visa-specified access to national haemophilia funding are excluded from the target patient group.

5. Background

This section provides an outline of the nature of the major inherited bleeding disorders, the internationally accepted comprehensive care model for haemophilia care and the current structure of inherited bleeding disorder services in New Zealand.

5.1 Inherited bleeding disorders

Inherited bleeding disorders comprise a heterogeneous group of conditions associated with an increased tendency to bleed either spontaneously or after provocation through trauma or medical intervention. The milder conditions are more common than the rare severe disorders. People with the severe disorders (predominantly severe haemophilia A or B), however, have complex medical needs and are the focus of the majority of health service input into these conditions.

There are estimated to be approximately 40,000 people with von Willebrand's disease and 400 people with haemophilia in New Zealand. Mild platelet function disorders probably occur with a similar frequency to von Willebrand's disease, but are rarely diagnosed in New Zealand due to limitations in current diagnostic facilities. Other bleeding disorders are rare.

5.1.1 Haemophilia

Haemophilia is bleeding disorder characterised by the isolated deficiency of either coagulation factor VIII (haemophilia A) or coagulation factor IX (haemophilia B). It is a rare condition affecting approximately 1 in every 10,000 live births. The frequency of haemophilia is the same across all ethnic groups. Approximately 30% of all new diagnoses of haemophilia are in people with no known family history of the condition (so called 'new mutations').

Depending on their factor VIII or IX level people with haemophilia may be classified as severe, moderate or mild. The normal range for factors VIII and IX is 50-150 iu/dl. People with severe haemophilia have FVIII or IX levels of less than 1 iu/dl, those with moderate haemophilia have levels of between 1-5 iu/dl and those with mild haemophilia have levels of between 5 and 40 iu/dl.

Patients with haemophilia typically bleed for longer than people with normal coagulation after injury or surgery, and those with the severe forms of the condition will also experience apparently spontaneous bleeding. Patients with haemophilia can suffer bleeding from any area of the body with a blood supply. Gastro-intestinal and intracranial bleeding may be life-threatening.

Bleeding most often occurs into joints or muscles, which is very painful and can have a temporary effect on the use and mobility of the joint or muscle. Recurrent bleeding into joints and muscles results in long-term damage in the form of haemarthrosis (blood induced arthritis) and muscular contractures, which in turn are associated with chronic pain and complications. These are the most common long-term adverse outcome for people with

haemophilia.

Acute pain associated with bleeding episodes and chronic pain due to musculo-skeletal damage are common and challenging problems faced by people with haemophilia.

Haemophilia and its treatment has a significant impact on the patient and family and can lead not only to physical disability but also to problems with schooling, employment and relationships.

Multiple members of a single family, male and female, over a wide age range may be affected by complications of haemophilia. In general, symptomatic female family members have a less severe factor deficiency than their affected male relatives. However, women of childbearing age with mild bleeding disorders can often suffer symptoms in the form of menorrhagia or postpartum bleeding and this can be quite severe for some. As the life expectancy of people with haemophilia increases, diseases of older age, including cancer, diabetes and cardiovascular disease, are increasingly complicating the management of their bleeding tendency.

Males with milder bleeding disorders bleed infrequently and generally only in relation to trauma or surgical procedures. They rarely require therapy with coagulation factor concentrates but will require urgent and expert care at times of acute bleeding following trauma, or when dental or surgical procedures are planned.

During the late 1970s and early 1980s the majority of regularly treated patients with haemophilia were infected with either HIV and/or hepatitis through treatment with blood-derived factor concentrates. This has led to profound medical and psychosocial problems and makes the delivery of future clinical care a particularly sensitive issue for patients and their families

Around 30% of patients with haemophilia A will develop an antibody against factor VIII, often referred to as an inhibitor. There is significant morbidity and mortality associated with inhibitor development. Inhibitors against factor IX are less common and occur in 1-3% of people with haemophilia B. In approximately half of the people who develop inhibitors the inhibitor is transient and of low titre (less than 5 Bethesda units) and therefore of little clinical significance. In other patients the inhibitor is of high titre (more than 5 Bethesda units) and these patients do not respond to factor VIII therapy, requiring alternative and particularly expensive bypass treatments.

The lives of patients and their families can be transformed by high quality care. For those with severe haemophilia effective prophylaxis and treatment with factor concentrates can prevent disability later in life. With appropriate therapy, a child born today with severe haemophilia can look forward to an excellent quality of life and a normal life expectancy, with the opportunity to contribute fully in family, social and workplace settings.

5.1.2 Von Willebrand's disease

Von Willebrand's disease is a term used to describe a group of related bleeding disorders characterised by a quantitative or qualitative deficiency of von Willebrand's factor, a protein that protects coagulation factor VIII from degradation in plasma and also performs an independent role in facilitating the binding of platelets to blood vessel walls. It is a common bleeding disorder, affecting up to 1% of the population.

Von Willebrand's disease may be classified as type I (quantitative deficiency), type II (qualitative deficiencies) or type III (very severe deficiency). Bleeding in type I and II disease is most often in the form of bruising, nosebleeds, gastrointestinal bleeding and bleeding from

the female genital tract (menorrhagia or post-partum haemorrhage). Excessive bleeding may occur from any site after injury or surgery. People with type III von Willebrand's disease, also suffer apparently spontaneous bleeding into muscles and joints and are at risk for chronic musculoskeletal damage.

Von Willebrand's disease is currently under-diagnosed due to lack of awareness in both medical and non-medical communities. As a consequence, many sufferers do not receive appropriate therapy, and may suffer from disabling symptoms of anaemia or excessive menstrual bleeding or undergo unnecessary surgical intervention such as hysterectomy.

5.1.3 Inherited platelet function defects

Platelet function disorders cause muco-cutaneous bleeding similar to that seen in von Willebrand's disease. Severe forms such as Glanzmann's thrombasthenia and Bernard Soulier disease are rare. Milder forms such as platelet storage pool disease are thought to occur with a similar frequency to Von Willebrand's disease.

Although diagnostic assays for the milder platelet function defects are established overseas, New Zealand laboratory facilities do not currently provide these and patients with these conditions are largely undiagnosed.

5.1.4 Other bleeding disorders

Inherited deficiencies of coagulation factors such as factor XI, VII, V, X, II are rare. Bleeding is most often associated with injury or surgery. Specialist knowledge is required in order to ensure that people with these disorders are protected from bleeding associated with trauma or medical interventions and also to ensure that inappropriate treatments are avoided.

Acquired coagulation factor deficiencies are also rare. Some conditions such as acquired haemophilia and acquired von Willebrand's disease are associated with life threatening bleeding and require urgent and specific treatment. The products used to treat these conditions are very expensive and also carry thrombotic risk. It is essential that they are managed by specialist staff with expertise in haemostasis.

5.2 Comprehensive Care

Effective management of the conditions described above is complex and requires collaboration between diverse specialists and health care professionals. Severe inherited bleeding disorders affect the whole family. There may be major psychosocial consequences for relatives of people with bleeding disorders as a consequence of their carrier status. In addition, family members of the index patient, may themselves have significant bleeding disorders.

For haemophilia the internationally and universally accepted model of management is "comprehensive care".

Comprehensive care requires care to be coordinated by a haemophilia treatment centre by a specialist haemophilia physician and nurse. This team are responsible for providing haematological management and for co-ordinating input from a group of diverse health professionals from other relevant specialties, who also have an interest in haemophilia. These specialties will include physiotherapy, paediatrics, orthopaedics, rheumatology, pain, infectious disease, gastroenterology, obstetrics and gynaecology, dental surgery, genetics, psychology, geriatric medicine, physiotherapy, and social work. Comprehensive care requires the support of a coagulation laboratory capable of providing specialist coagulation tests on both a routine and urgent basis.

Instituting comprehensive care has been shown to significantly improve health outcomes for

people with haemophilia, as well as dramatically reduce time lost from school or work, hospital admissions, cost of care and unemployment amongst people with haemophilia (Kaspers CK & Dietrich SL 1985, Lippert et al 2005).

The NHMG, NZTG and HFNZ (www.haemophilia.org.nz) endorse the comprehensive care model for haemophilia in line with recommendations of the World Federation of Haemophilia (www.wfh.org).

5.3 *The need for national service specifications*

Most inherited bleeding disorders are uncommon conditions. All require specialist expertise for the provision of safe and effective care. Few health professionals have the relevant knowledge and experience to be able to deliver appropriate care for this group of patients. Poor management of bleeding disorders results in serious adverse clinical consequences, including lifelong disability and death.

Internationally haemophilia is considered to be one of the world's most expensive disorders to treat because of the cost of the therapeutic products and the lifelong nature of treatment. Historically, where bleeding disorders have been treated by carers other than experienced haemophilia clinicians, there have been cases of under and over-prescription of therapeutic products leading to poor outcomes.

The consequences of past treatment, including insufficient access to therapeutic products, the inability to undertake surgery and the inability to treat the consequences of haemophilia, is still impacting on the current management of health services in New Zealand.

This specification is written at a time when haemophilia care is evolving in response to the introduction of new technologies. Together with improved ways of managing haemophilia care, the introduction of longer-acting formulations of factor concentrates will provide new challenges to services for people with bleeding disorders in New Zealand within the next few years.

Delivery of clinical care across the country needs to be equitable. A uniform, national service specification that sets out the standards of care for patients with inherited bleeding disorders will facilitate equitable access to an appropriate range of clinical and laboratory services. This service specification is intended to be adopted as the national service framework, in keeping with government initiatives to establish service frameworks for specialised disorders.

5.4 *Structure and governance of haemophilia services in New Zealand*

5.4.1 *Treatment Centres*

There are six Haemophilia Treatment Centres (HTC) situated within haematology departments of tertiary level hospitals and supported by District Health Boards (DHBs). Services are largely funded by the DHB managerially responsible for these Hospitals. However, specialist haemophilia nurses in every centre and specialist physiotherapy positions in three of these centres are funded from central National Haemophilia Management Group (NHMG) funds.

The 6 regional centres are based in: Auckland, Waikato, Palmerston North, Wellington, Christchurch and Dunedin

5.4.2 NHMG

The management of haemophilia and the rarer bleeding disorders provide some unique challenges in a country with a small population spread over a wide geographical area. The disease prevalence is low and, at the same time, specialist teams with experience in the management of bleeding disorders are required to provide appropriate care for this group of patients. Inappropriate, inadequate or delayed treatment results in high morbidity, mortality and health care expenditure. Therefore expert care must be readily accessible by patients for both routine reviews and emergency therapy. Treatment costs are high and individual patients may show wide fluctuations over time making financial planning difficult for individual DHBs.

Since July 2006, governance of haemophilia services and funding for haemophilia treatment products has been the responsibility of a multidisciplinary committee, the NZMG. NZTG, HFNZ, the New Zealand Blood Service and DHBNZ are all represented on NHMG.

The majority of the budget is reimbursed via the community pharmaceutical budget. The rest is contributed on a per capita basis by all New Zealand DHBs. This Budget is then managed by the NHMG. The six treating DHBs are reimbursed from this fund for the cost of treatment products. Other costs, such as staffing, provision of inpatient and outpatient facilities, surgery and treatment of non-bleeding complications including hepatitis and HIV are primarily funded by treating DHBs.

NHMG is responsible for ensuring optimal provision of services to people with haemophilia and related disorders whilst keeping expenditure within the financial limitations agreed with DHBNZ. Where funding limitations allow, terms of reference permit investment from the NHMG budget to provide future improvements in the service to patients with haemophilia and related disorders within New Zealand. This mechanism has made it possible to employ specialist haemophilia nurses in every NZ HTC and to provide regional access to specialist haemophilia physiotherapy.

The NHMG has also facilitated the development of a national database for patients with bleeding disorders and has successfully collaborated with PHARMAC in the tendering process to moderate the cost of treatment products. Also in providing access to safer medication for the treatment of arthritic pain in haemophilia.

This model of care is currently unique within New Zealand and provides an effective mechanism for ensuring equity of resource allocation the same time as optimizing efficiency of resource use.

5.4.3 NHTG

All specialist medical, nursing and physiotherapy staff are members of the NHTG. This body has the responsibility of developing and maintaining national treatment guidelines and to provide peer review for case management. This group also serves as a medical advisory group to the NHMG. NHTG holds regular business and educational meetings.

5.4.4 HFNZ

HFNZ is a charitable organisation that was established in 1958 to serve the needs of people with haemophilia and other related bleeding disorders. As an organisation it seeks to provide support to patients and their families affected by bleeding disorders and to provide representation of the patient's perspective at government and health service provision level.

HFNZ provides patient advocacy together with social, financial and educational support for its members. HFNZ community-based outreach workers deliver a national service and liaise with the hospital-based treatment centres in the care of patients with haemophilia and related

disorders. The majority of funding for the outreach service is provided by HFNZ with a contribution being provided by DHBNZ.

5.4.5 NZBS

NZBS stores and dispenses plasma-derived treatment products on request from haemophilia treaters for people with bleeding disorders. In some centres they also handle and dispense recombinant Factor VIII, V, IX and VIIa and the commercially produced plasma product FEIBA.

6. *National service principles and standards*

This section outlines some important guiding principles and standards on which the New Zealand national bleeding disorder service is based.

Details of the requirements for service provision at HTC's are outlined in section 7.

6.1 *Diagnosis*

Bleeding disorders may present with chronic symptoms or as an emergency. It is essential therefore that the definitive diagnosis of bleeding disorders is available within a time frame appropriate to the presentation of the disorder. Without a full and accurate diagnosis it is not possible to determine effective therapy for the treatment or prevention of bleeding. All people with suspected bleeding disorders should have access to a diagnostic service that can make a precise laboratory diagnosis of the severe and common bleeding disorders in a clinically appropriate time frame.

6.2 *Access to Treatment*

Specialist expertise is necessary to ensure that patients with bleeding disorders are treated in a safe, effective and cost-effective manner.

Clinicians without specialist haemostasis expertise may not fully appreciate the necessity for specific measures required to diagnose, prevent and treat bleeding in patients with bleeding disorders. They may overlook the possibility of internal bleeding as a cause of acute illness and may not recognise the potential for serious harm or death from bleeding associated with minor trauma, invasive procedures such as endoscopy or surgery in these patients. Failure to engage with a specialist haemostasis service at an early stage can have severe consequences for the patient and their family.

Pregnancy and obstetric delivery pose particularly challenging bleeding risks with both mother and baby's lives at stake. The management of neonates with bleeding disorders differs from routine neonatal management. The consequences of failing to diagnose and appropriately manage a bleeding disorder in a neonate can result in death or lifelong disability.

Inherited bleeding disorders are lifelong conditions and the relationship between patients, their families and the people looking after them is critical.

- All people with a suspected significant bleeding disorder should be referred to a comprehensive care HTC for diagnosis and management.
- Access to the haemophilia treatment centre should be available on an emergency basis for patients with active bleeding and on an urgent basis for patients with bleeding disorders who are pregnant or who are scheduled for invasive procedures

- or surgery, including dental surgery.
- A female carrier who is expecting a baby who may be affected by a bleeding disorder should be referred urgently to the HTC to facilitate prompt diagnosis and appropriate management of the neonate
- The birth of a baby who may be affected by a bleeding disorder should be reported immediately to the HTC to facilitate prompt diagnosis and appropriate management of the neonate
- Patients should have the right to transfer between centres, even if this means attending a centre that is not geographically the closest to them.
- Adequate diagnosis, treatment and on-going care of people with bleeding disorders should be provided in compliance with the standards outlined in the NZTG Guidelines for Treatment of Haemophilia.
- Foreign visitors will be afforded emergency treatment only, unless visa-specified eligibility for publicly funded health and disability services.

6.3 *Choice of coagulation factor concentrates*

Treatment for bleeding disorders will often require the administration of coagulation factor concentrates. These are manufactured from either human blood donations (plasma-derived concentrates) or from animal cell tissue culture transfected with the relevant human gene (recombinant factor concentrates).

Historically plasma-derived products have transmitted hepatitis B, hepatitis C and HIV to patients with bleeding disorders. Modern preparations carry a very low risk of transmitting these agents. However, current measures may not protect patients from newly emerging, as yet unidentified, infectious agents. For this reason, recombinant products are considered to have a potential safety advantage over plasma-derived products. Currently, recombinant products are available for FVIII, FIX and FVIIa.

For the minority of people with neutralizing antibodies (inhibitors) to standard factor VIII or IX concentrates, simple replacement therapy will be ineffective and treatment with bypassing agents, either recombinant FVIIa (rVIIa) and plasma-derived factor eight bypassing agent (FEIBA) will be available. The two agents are not interchangeable as the relative efficacy of the two agents varies between patients, and also because rVIIa and FEIBA have different durations of action.

At the present time, factor replacement therapy for von Willebrand's disease is only available in plasma-derived form. Recombinant von Willebrand's factor may be available in the near future.

rVIIa may be used to treat FVII deficiency, FXI deficiency and may also be beneficial in the management of some platelet disorders. However, for many of the rarer bleeding disorders recombinant products are not currently available and plasma-derived products will be required for the treatment and prevention of bleeding.

- Recombinant coagulation factor concentrates to be offered as treatment to all new cases of haemophilia.
- Recombinant products are viewed as having potential safety advantages to plasma derived products and as such all children with haemophilia should be offered treatment with recombinant products.
- Children with haemophilia who have been treated with recombinant products to continue on recombinant products into and throughout adult life.
- Contracts for the purchase of recombinant FVIII products from at least two manufacturers to be maintained at all times with the aim of securing a medium-term

supply of recombinant FVIII to New Zealand in the event of an interruption in supply from one manufacturer.

- Recombinant coagulation factor concentrates should be offered to treat adult patients with haemophilia who have not previously received plasma-derived products.
- Recombinant products should be offered to adult patients with haemophilia who have previously been treated with plasma-derived factor VIII or factor IX.
- Recombinant coagulation factor concentrates to be offered to treat symptomatic female carriers for surgery or invasive procedures.
- Plasma derived concentrates to be used to treat adult patients previously treated with plasma-derived product provided they have been offered recombinant product(s) and wish to remain on a plasma-derived product.
- Patients with haemophilia and inhibitors to be treated with either recombinant VIIa or a plasma-derived bypassing agent for bleeding episodes.
- Plasma-derived factor VIII-containing von Willebrand's factor is currently used to treat patients with von Willebrand's disease where factor replacement is required.
- Where possible, recombinant products should be used for the treatment of the rarer coagulation deficiencies.

6.4 Prophylaxis

Prophylaxis is the regular administration of intravenous factor concentrates given to patients with severe and moderately severe haemophilia and type III von Willebrand's disease to prevent acute episodes of bleeding into joints and muscles. Prophylactic therapy given 2-3 times a week from an early age can prevent long term musculoskeletal damage, avoiding disability and the need for remedial surgical and medical treatments later in life. It also reduces the amount of disruption to education, work, social and family life caused by unpredictable bleeding episodes.

- Prophylactic therapy should be made available for a child with severe haemophilia after his first significant bleeding or by the age of 3 years.
- The introduction of prophylactic therapy must be an individual decision and based upon the patient's and the family's particular circumstances.
- The duration of prophylactic therapy will usually be at least until late adolescence and the decision to continue or discontinue prophylaxis after this age will depend upon individual clinical circumstances. Prophylaxis may be continued into adulthood.
- Prophylactic therapy may be initiated in the hospital outpatient setting, but will usually be routinely administered by the patient or family member(s) in the home setting with clinical and psychosocial support from their HTC.
- Prophylactic home therapy represents a major undertaking for the parents of a child with haemophilia and should ideally only be embarked upon when well coordinated by the HTC and the family. Carers should be familiarised and willing to accept responsibilities for these treatments, competent at delivering them and will undertake to provide the haemophilia centre with the relevant clinical information concerning the use of coagulation factor concentrates in the home setting.
- Secondary prophylaxis is also recommended for adults who are not receiving longterm prophylaxis where there has been recurrent bleeding into a single joint, often referred to as a 'target' joint.

6.5 Home and community care

Home treatment administered by parents and people with haemophilia facilitates the prompt treatment of bleeding, which can both reduce the amount of treatment required to control

bleeding and also reduce the risk of long-term musculoskeletal complications. Prophylaxis also minimises the effect of the bleeding disorder on absence from school and work and reduces the impact of the condition on leisure activities for sufferers and their families. Accurate record keeping regarding the use of product in the home and any breakthrough bleeding is essential to inform the development of optimal treatment programs and to reduce wastage through inappropriate use or expiry of treatment products. The involvement of HFNZ, an established, well informed patient group can be helpful in providing families with educational and social support for home therapy.

- Wherever appropriate, the routine treatment (prophylaxis and on demand therapy) of people with haemophilia should be delivered in the home setting.
- Treatment for severe bleeding episodes may, however, require hospital admission and access to the HTC.
- Under usual circumstances, a patient with severe haemophilia should be on home treatment by the age of 4 years at the latest, depending on venous access and family circumstances. However, if treatment cannot be managed appropriately in the home setting, it should take place in the hospital setting.
- Children and adults with haemophilia and their carers should be encouraged to be active participants in the delivery of care.
- Patients and their families will be educated on the importance of keeping formal records of all treatments and episodes of bleeding.
- Usage of coagulation factor concentrates and record keeping in the home setting will be monitored by the HTC.
- Where consent is given by a person with haemophilia (or their carer in the case of a child) HTCs will collaborate with the patient group, HFNZ, to facilitate effective haemophilia care in the community.

6.6 *Treatment of children*

Management of children with bleeding disorders must adhere to principles that apply to paediatric healthcare in general. The specific psychological, social and developmental needs of children must be respected. Knowledge and experience in the management of specific paediatric concurrent healthcare issues is also required from health carers in the paediatric setting.

Transfer from paediatric to adult care is a particularly difficult time for the teenager with haemophilia.

- The care of children with haemophilia and related disorders should be supervised by staff trained and experienced in the management of children
- Outpatient review, inpatient wards and treatment areas should be appropriate to the needs of children and adolescents.
- The transition to adult care should be seamless process occurring over an appropriate period of time and handled sensitively allowing the process to be achieved by an appropriate age.

6.7 *Female patients and asymptomatic carriers*

A common misconception is that haemophilia, because it is inherited in an X-linked manner, is a disorder that affects only males. However, because of a process known as skewed lyonisation, some female carriers of haemophilia also have low levels of factor VIII or IX. Most symptomatic females will have mild haemophilia. A few girls and women have very low factor levels and suffer from moderate or severe haemophilia. Other bleeding disorders

affect males and females equally in terms of factor levels.

The effect of bleeding disorders is often different for males and females. Women with bleeding disorders not only experience the same haemorrhagic symptoms as males with similar factor levels, but also face additional problems associated with heavy menstrual bleeding and obstetric bleeding, predominantly post-partum haemorrhage.

A variety of reproductive options are available to families who are at risk of having children with inherited bleeding disorders. Women with severe inherited bleeding disorders and female carriers of severe haemophilia, together with their partners, can choose to avoid having an affected child through a range of options including pre-implantation genetic diagnosis with assisted reproduction and antenatal diagnosis through chorionic villous sampling or amniocentesis with consideration of termination of pregnancy. In some situations other options such as egg donation or adoption may also be considered.

Because of the huge practical and emotional demands on a family associated with having a boy with severe haemophilia, it is not uncommon for the bleeding problems and potential carrier status of female relatives to go unrecognised and untreated.

- Women with bleeding disorders should have access to the same range of bleeding disorder services as men.
- They also require appropriate collaboration between specialist haemostasis staff and obstetricians and gynaecologists with an interest in bleeding disorders to ensure optimal management of the special bleeding problems associated with menstruation and childbirth.
- Expert genetic advice and counselling are required to inform families of the genetic implications of a diagnosis of haemophilia or relate bleeding disorder and to allow families to make informed choices regarding the reproductive options available to them.
- A reliable system for identifying all female carriers of haemophilia and informing them of their carrier status and reproductive options must be available to clinicians involved in the care of families with bleeding disorders.

6.8 *People with haemophilia and inhibitors*

The management of patients with inhibitors is complex and treatment products are particularly expensive.

Treatment for bleeding requires the use of bypassing agents, either FEIBA or rVIIa. Bypassing agents are considerably more expensive than the FVIII and FIX concentrates that would be used in non-inhibitor patients in the same situation. Surgery in patients with inhibitors can be performed safely with the use of either FEIBA or rVIIa to maintain haemostasis.

People with haemophilia who have a newly diagnosed inhibitor, particularly children, are likely to benefit from immune tolerance programmes. Tolerisation is the use of chronic exposure to high doses of the factor VIII or IX to which the patient has inhibitors, with the aim of inducing immune tolerance to the coagulation factor (i.e. loss of the neutralising antibody). This typically takes approximately 12-18 months and requires the regular administration of very large amounts of coagulation factor concentrates. Immune tolerance programmes are very expensive and expose people with haemophilia to large amounts of products.

Similarly, short or long-term prophylaxis against bleeding in inhibitor patients using regular bypassing agents would incur a much higher cost than prophylaxis against bleeding with FVIII or FIX concentrates in non-inhibitor patients. There is evidence to suggest that bleeding episodes are reduced and quality of life improved by using prophylactic bypassing

agents in people with haemophilia and inhibitors, but evidence that this approach reduces long-term complications is currently lacking.

- Immune Tolerisation, and surgery in people with haemophilia and inhibitors should be carried out only in centres that are experienced in these forms of therapy and that have appropriate clinical and laboratory resources.

6.9 Māori

Māori appear to be affected by haemophilia at a similar rate to other ethnicities. They have specific cultural values and beliefs. These need to be recognised and countenanced in order to ensure the provision of effective and culturally appropriate services for Māori with congenital haemorrhagic conditions.

- Services must ensure cultural safety for all clients, including Māori.
- The principles of the Treaty of Waitangi must be observed.
- Services will be provided in a way that will contribute to the objectives of He Korowai Oranga – the Māori Health Strategy as referred to in the New Zealand Health Strategy.
- Service providers will consult and include Māori in service design through Piri Toto, the Māori representative group within HFNZ

6.10 A National Service

Optimising care for rare disorders that require expert management and expensive treatment products in a country with a small population spread over a wide geographical area is challenging.

The model favoured by the NZTG and NHMG is the development of a national bleeding disorder service with treatment delivery continuing to be provided at the existing six haemophilia centres. Several important components of a national service (outlined in section 5.4) are already in place for the treatment of people with bleeding disorders. It is anticipated that the provision of bleeding disorder services, whilst continuing to deliver patient care at or close to the patient's home, will increasingly be planned and co-ordinated on a national basis.

A national service framework would address the challenges outlined above and provide opportunities for more effective negotiations with suppliers of treatment products and pharmaceuticals.

- A National service aims to provide equity of access to treatment and consistency of clinical management approach across all New Zealand centres.
- The national service requires the establishment and maintenance of an accurate profile/database of patients with inherited bleeding disorders in New Zealand and the distribution of such patients between treatment centres.

6.11 High cost procedures

Some special situations exist in the treatment of people with haemophilia for which treatment carries a particularly high financial cost. At the present time, very high cost treatments will usually be one of the following:

1. Immune tolerance therapy for people with haemophilia and inhibitors.
2. Surgery in people with haemophilia and inhibitors
3. Prophylaxis against bleeding in patients with haemophilia and inhibitors.

With the development of new treatment products and possibly genetic therapies, other high

cost treatment options may become relevant considerations in the future.

- Planned high cost procedures such as immune tolerance programmes, prophylaxis in people with haemophilia and inhibitors and elective surgery in people with haemophilia and inhibitors should only be undertaken after discussion with NZHTG and NZHMG and majority approval from these groups.
- Emergency high cost procedures will be initiated in line with current New Zealand haemophilia treatment guidelines without the need for prior discussion with NZHTG and NZHMG and will be discussed with these groups at the earliest opportunity.
- New therapies incurring similar high cost from the central haemophilia budget will be discussed with NZHTG and NZHMG and approved by these groups prior to their use at HTC.

6.12 Patient responsibilities

Patients with bleeding disorders who require frequent treatment for bleeding or prophylactic treatment to prevent bleeding will ordinarily be enrolled in a home therapy programme. Patients or their carers will be trained to administer home treatment and be entrusted with supplies of factor concentrate on a regular basis. There is an expectation that records of bleeding episodes and treatment usage, which greatly facilitate future treatment planning, will be provided by those on home treatment. Treatment products have a limited shelf life and it is important that product is not allowed to expire in the home setting as expired product cannot be used for treatment. This is particularly relevant in the context of financial constraints that limit treatment options for some patient groups.

- People with haemophilia who are on home treatment have an obligation to behave responsibly and manage factor storage, usage and the maintenance of appropriate records of product use. In conjunction with their HTC.

7. Standards of diagnostic services and treatment delivery at HTCs

This section addresses the requirements for diagnostic and treatment service provision at HTCs.

Details of recommended treatments for individual patients are described in the national treatment guidelines for the delivery of haemophilia care.

7.1 Referral from primary and secondary care

Patients with bleeding disorders may present for the first time to one of a wide variety of clinical practitioners. Most clinicians will have insufficient specialist knowledge or experience to be able to diagnose or treat these patients effectively.

Delayed referral to the appropriate specialist may also result in delayed, ineffective or potentially harmful therapy being used

- Clear, written processes for routine, urgent and emergency referral of new suspected cases of bleeding disorders and new bleeding episodes in people known to have bleeding disorders need to be in place and to be made known to primary and secondary care medical and nursing staff.

7.2 *Diagnosis*

Failure to obtain a precise diagnosis in a bleeding disorder in a timely manner can cause unnecessary disability and death. There is also a risk that ineffective or potentially harmful therapy may be used while the diagnosis is unclear.

- HTCs must have an onsite laboratory capable of providing a 24 hour a day, 7 days a week specialist coagulation diagnostic service.
- The ability to detect coagulation defects including haemophilia A and B, Inhibitor screening, von Willebrand's disease, Acquired haemophilia and rare factor deficiencies, including inhibitors, must be available on a 24 hour, 7 day a week, emergency basis.
- All laboratory staff responsible for reporting routine coagulation screens at the HTC must be competent to identify coagulation abnormalities encountered during screening that suggests the presence of a bleeding disorder.
- On site duty staff must be able either to perform further specialist testing to elucidate the reason for an abnormal coagulation screen or be aware of the need to call in someone who will do so urgently, if clinically indicated.
- Those laboratories participating in genetic analysis must have :- the facilities and expertise to identify haemophilia mutations; the ability to assign carriership and make antenatal diagnosis; and, a turnaround time of 6 weeks for routine samples and two weeks for urgent samples.

7.3 *Initial specialist assessment*

- History, examination and laboratory diagnosis
- Communicate diagnosis and treatment options, including written information in appropriate language
- Treatment plans
- Issue patients with special medical cards giving details of their inherited coagulation disorder, treatment information and haematology contacts.
- Inform of symptoms requiring emergency and urgent medical assessment and how to access services
- Refer to other specialists as required
- Establish family tree and identify other family members that may be sufferers or carriers
- Inform of HFNZ, medic alert

7.4 *Acute Services*

- Due to the relatively rare nature of bleeding disorders there is a risk that patients with haemophilia may not be treated appropriately when they present out of hours to an Accident and Emergency Department. Effective treatment is more appropriately administered promptly and efficiently if the specialist haemostasis team is involved as soon as it is recognised that a bleeding disorder may be present.
- Emergency treatment should be available on a 24 hour basis for patients with haemophilia and related disorders.
- A 24 hour advisory and response service for general practitioners, dental surgeons, hospital doctors, patients and families.
- There should be a consultant haematologist on-call at all times with responsibility for patients with haemophilia.
- Children with haemophilia should have 24-hour access to a paediatric ward or setting for the purposes of acute treatment of severe bleeding episodes and

surgical interventions.

- Specific treatment plans for managing acute bleeding episodes should be accessible and regularly updated.
- Patients should be given clear information as to who they should contact in the event of an emergency.
- All patients should be issued cards verifying essential diagnostic and management details to facilitate rapid emergency department processing in the event of presentation to hospital with an acute bleed.
- On-call arrangements for haemophilia should be clearly identified to junior hospital medical staff and triage nurses.
- Junior medical staff responsible for care of haemophilia out of hours should receive formal education about haemophilia and its treatment.
- A protocol for the management of patients with haemophilia out of hours should be available for junior medical staff.
- There must be appropriate laboratory back up for the emergency care of patients with haemophilia and related disorders.
- Clear lines of communication between the medical and nursing staff at the treatment centre and the local district hospital as well as liaising with affiliated HTCs and appropriate community agencies.

7.5 *Planned management*

7.5.1 *Outpatient review*

All registered people with inherited bleeding disorders should be offered on-going and regular clinical review, with records kept of non-attendance.

- People with severe/moderate haemophilia should be reviewed at least 6-monthly.
- People with mild haemophilia and other inherited bleeding disorders should be offered a review yearly.
- People with haemophilia who have frequent bleeding, inhibitors, chronic musculoskeletal damage or viral complications of previous treatment are likely to require more frequent review.
- Patients with haemophilia receiving treatment should be screened on a regular basis for the presence of an inhibitor.
- All patients with inherited bleeding disorders who are likely to require blood and coagulation factor concentrates should be offered vaccination against hepatitis A and hepatitis B if not already immune.
- Patients with severe/moderate haemophilia should be reviewed by a physiotherapist with responsibility for haemophilia patients for a joints scoring/measuring assessment once a year. This data should be used to form rehabilitation plans, as required, to seek to maintain joint movement and general mobility.
- Patients with joint and musculoskeletal issues should have access to rheumatology services
- Joint haemophilia-orthopaedic clinics should be available on at least an annual basis for all patients with known or suspected musculoskeletal damage
- Timely access to specialist pain management services should be available
- It is essential that patients with HIV or hepatitis infection are referred to an appropriate specialist and that treatment strategies are in accordance with published guidelines.
- Patients and families should have access to social worker and counselling as required.
- Patients should have access to appropriate dental services

7.5.2 Home therapy

- Home treatment training programmes including home and school visits where appropriate.
- Patients and their families will be educated as to the importance of keeping formal records of all treatments and episodes of bleeding
- Haemophilia centres will monitor the usage of coagulation factor concentrates
- Home treatment has implied responsibilities for both patient's and their families and for the HTC. If helpful contracts can be put in place to help clarify these responsibilities.

7.5.3 Prevention of bleeding in association with medical interventions and surgery

- Treatment plans for maintaining haemostasis through elective surgical and dental procedures should be created and distributed to involved parties before the procedure.
- Interaction with specialist teams within the hospital to coordinate care for haemophilia patients undergoing surgical, dental and obstetric procedures.

7.5.4 Prevention of bleeding in association with pregnancy and delivery in female carriers of haemophilia

Pregnancy is a potentially serious undertaking in haemophilia as both the mother and infant may be at increased risk of bleeding.

- It is essential that the obstetric management of women with inherited bleeding disorders and known carriers of haemophilia should be carried out in (or in association with) HTCs that have expertise in this area.
- A documented care plan for the delivery of the infant should be established.
- There must be close collaboration between the obstetric team and the haemophilia centre at all stages of the pregnancy.
- Postnatal confirmation of the diagnosis should be carried out as soon as possible.

7.5.5 Carrier detection, genetic diagnosis and reproductive choices.

- Factor VIII or IX assays should be carried out on all carriers of haemophilia. Those haemophilia carriers with low factor VIII or IX levels should be formally registered with a haemophilia centre and subject to regular review in the same manner as patients with mild haemophilia.
- Genetic counselling should be available before, during and after the process of haemophilia genetic analysis.
- A fully documented pedigree study should be carried out for each family, allowing identification of obligate carriers, possible carriers and non-carriers.
- Intragenic polymorphism and linkage analysis and/or direct gene analysis should be carried out to establish carriership for female members of the family where there is a patient with haemophilia.
- Following a diagnosis of carriership, there should be specialised genetic counselling and education so that carriers can understand the transmission of haemophilia within their own family.
- It is recommended that a network of genetic testing centres be established that can provide nationwide genetic analysis in haemophilia and related disorders.
- All patients with haemophilia should have mutation detection carried out.
- It is recommended that carriers receive formal education about the transmission of haemophilia within the family before starting a pregnancy, if at all possible.
- There should be access to an expert foetal medicine unit for discussion of antenatal diagnosis and pre-implantation diagnosis.

7.5.6 Collaboration with other services

Haemophilia centres will coordinate the delivery of haemophilia services, in hospital and in the community. This will require the haemophilia centre to communicate effectively with other agencies, especially the patient representative organisation HFNZ.

- HTC's will provide access to advice for patients, their families, other health providers and agencies.
- A shared care protocol should be developed between the secondary and tertiary centres where appropriate.
- A small number of carriers of haemophilia were infected with hepatitis or HIV. These patients require access to the same range of services as described for virally infected patients with haemophilia.
- With the permission of the person with the bleeding disorder, HTC's to collaborate with HFNZ outreach service to provide educational, psychosocial and financial support.
- Access to kaumatua/kuia/cultural support advocacy should be provided for Māori consumers.
- Information for schools and workplaces to be provided on request.

7.5.7 Transferring between haemophilia treatment centres

- For patients who are moving between treatment centre catchment areas for short periods of time, appropriate shared care planning should be instigated.
- Where patients are transferring permanently between centres a formal written transfer document must be provided by the referring centre.
- Where paediatric services are provided separately from adult services the transfer between paediatric and adult services will also require a formal transfer process.

8. Other functions of haemophilia centres

8.1 Education

- Educational programmes for medical and nursing staff, biomedical scientists and related paramedical personnel.
- Educational programmes, monitoring and support for patients and their families concerning all aspects of home therapy and community care are arranged and managed via the patients HTC. HFNZ play a vital supporting role in educating and advocating for patients in the community environment..
- Written educational material in an appropriate language, where possible, to be developed in collaboration with HFNZ.

8.2 Support for secondary and primary care

Close liaison is required between the treatment centre and external hospitals. Shared care may be coordinated by a haematologist, general physician or paediatrician at the district hospital.

The following should be provided at the local district hospital as required:

- Outreach clinics.
- Joint clinics with local haematologists and paediatricians.
- Local treatment plans for the management of acute bleeding episodes that should

- be available with the local emergency department.
- Education for nursing and medical staff at district hospitals.
- A process for rapid referral of new suspected cases of bleeding disorders.
- Clear lines of communication between the medical and nursing staff at the treatment centre and the local district hospital.

8.3 Record keeping

- All haemophilia patients should be registered with a HTC.
- Each HTC should maintain a register of all patients with inherited bleeding disorders attending the centre.
- Informed consent will be obtained from patients for clinical details to be held on the HTC patient register and the NHMG national database.
- Patients on home therapy will submit data on bleeding episodes, treatment with coagulation factor concentrates and treatment outcomes to their HTC on a regular basis as a condition of an agreed contract for home treatment.

All centres delivering haemophilia care should collect detailed information concerning the outcome of treatment. This should include the following:-

- The total coagulation factor concentrate received by each patient per year.
- Patient's weight
- The total number of treatments received by each patient each year.
- The amount of coagulation factor concentrate given for prophylaxis and emergency therapy.
- Whether the patient is on home therapy.
- The number of breakthrough bleeds on prophylactic regimens.
- The number of days spent in hospital due to haemophilia.
- The number of days missed at work/school due to haemophilia.
- Any surgical procedures carried out.
- Evidence of joint and muscle damage by both clinical and radiological assessment.
- Annual joint score measurements

Outcome data should form part of an annual report that will also include information on clinical audit activities.

8.4 Audit

Participation in clinical audit is considered to be an important component of the work of an HTC.

- Services will implement processes including retrospective case review and analysis of treatment pathways, leading to more effective and efficient resource utilisation and improved health outcomes
- NHMG working with NZTG will establish and maintain a national bleeding disorder database and will undertake to provide annual reports at a national level on the performance of the service for people with haemophilia and related bleeding disorders.
- Māori client satisfaction surveys will be performed.

8.5 Research

- Participation in clinical trials
- Participation in research and development

8.6 Contribution to a national haemophilia service

All six HTC's are expected to have an active role in the clinical governance of the national haemophilia service.

- Haemophilia specialist staff are expected to participate in NZTG discussions.
- HTC's will report projected and current high cost treatments to the NZTG.
- HTC's will register all patients with inherited bleeding disorders with the NHMG national database.

9. Staffing and Facilities

The wide-ranging needs of people with haemophilia and their families are best met through the coordinated delivery of comprehensive care by a multidisciplinary team of healthcare professionals.

In order to provide the services outlined above, the following staff and facilities should be available on site at each treatment centre:

9.1 Staffing

9.1.1 Medical

- Haematologists with appropriate training and experience in the management of bleeding.
- Paediatrician
- Physicians with expertise in the management of infectious disease including HIV and hepatitis.
- Pain specialist
- Rheumatologist with an interest in the musculoskeletal complications of bleeding disorders
- Orthopaedic surgeon with an interest in the diagnosis and management of the musculoskeletal complications of bleeding disorders
- Dental surgeon
- Obstetrician
- Gynaecologist

9.1.2 Nursing

Specialist haemophilia nurses with training in the care of patients with bleeding disorders are central to the provision of comprehensive care. The haemophilia nurses coordinate treatment, train patients and families for home therapy, organise supplies of coagulation factor concentrates and provide education of patients and their families. Haemophilia nurses also provide education for other health providers as well as schools and workplaces.

9.1.3 Allied health

- Physiotherapist with responsibility for haemophilia patients, who offers a range of acute treatments for patients with active bleeding and is responsible for rehabilitation, monitoring joint function and improving joints and muscles on a long term basis. All registered patients should be offered annual physiotherapy review as per WFH guidelines for comprehensive care centres. Annual assessments are performed using standardised assessment document as per WFH guidelines for comprehensive care centres.
- Social worker and HFNZ Haemophilia Outreach Worker, with responsibility for

haemophilia patients. People with haemophilia have significant lifelong social needs, and may require advice around welfare benefits as well as psychosocial support.

- Laboratory scientists with appropriate specialist coagulation training and experience involved with diagnosis and treatment monitoring
- Genetic counselling and diagnosis, in conjunction with specialised laboratories.
- Counselling and clinical psychology for patients and their families.

9.1.4 Administrative and support staff

- Reception staff
- Secretarial staff
- Data manager

Data handling for the delivery of haemophilia care can be complex and it is strongly recommended that all haemophilia centres are provided with the administrative resources to generate this information

9.2 Facilities

- Provision of appropriate storage and dispensing facilities for coagulation factor concentrates, both for hospital treatment and home therapy programmes.
- There should be dedicated facilities for disabled car parking in the vicinity of the haemophilia treatment centre.
- There should be appropriate parking and access for the disabled throughout the haemophilia treatment area.
- Accommodation, facilities and staffing should be appropriate to the needs of children and adolescents with bleeding disorders.
- Children with haemophilia should have 24 hour access to a paediatric ward or setting for the purposes of acute treatment of bleeding episodes.
- The clinical treatment of patients with haemophilia should take place in a dedicated clinical area that should be comfortable, quiet and appropriately equipped. These areas must allow confidential interviews between staff and patients.
- Routine treatment of patients with haemophilia in an accident and emergency department is not recommended.
- Access to whānau accommodation will be provided.
- Diagnostic and reference coagulation laboratory service, performing a full range of laboratory tests for the diagnosis and monitoring of inherited and acquired disorders of haemostasis (appendix 1).
- Specialist coagulation laboratory testing must be available on site within the hospital in which the treatment centre is located.
- Access to specialist coagulation testing and interpretation must be accessible as an emergency, 24 hours 7 days a week to ensure safe management of acute complications in people with bleeding disorders.
- HTC's should have the capacity to participate in clinical trials, research and development

10. Quality Standards

10.1 Bleeding disorder service.

Patient management should be in line with national haemophilia treatment guidelines and those issued by the World Federation of Haemophilia.

10.2 Professional guidelines

Medical, nursing and physiotherapy standards must comply with national professional guidelines

10.3 Laboratory standards

- All laboratory testing should be monitored via an appropriate established quality assurance programme (RCPA or NEQAS levels 1 and 2 for haemostasis). Persistently poor performance must be addressed and rectified as a matter of priority.
- All laboratories should have full accreditation through International Accreditation New Zealand (IANZ) medical laboratory testing scheme.

11. Monitoring service performance

- It is recommended that a process of formal external audit be established for all haemophilia centres, administered by NHMG and NZTG in conjunction with regional haemophilia networks and local patient groups. Centres will then be formally accredited as Comprehensive Care Centres or Haemophilia Centres, provided that they satisfy established criteria.
- All audits should be carried out according to a national audit framework. A suggested audit template is attached as appendix 4.
- The audit should appraise an agreed range of clinical and laboratory activities. Audit topics and the general form of the audit should be approved with health authorities and service providers and should also include input from members of the local patient group and other service users.
- Results of audits should be open and transparent and made available to relevant stakeholders.

12. Service agreements

Individual DHBs will provide and maintain appropriate facilities and staffing at the six HTC's to enable the provision of the services and treatments outlined above, including research and audit activity.

NHMG currently funds the salary of 4.5 FTE haemophilia nurses and 1.5 FTE specialist haemophilia physiotherapists.

NZBS will contract to provide, store and dispense CSL plasma-derived treatment products for all centres and recombinant products manufactured by other commercial suppliers at the request of a DHB. The host DHB for an HTC may elect to store recombinant treatment products in an alternative suitable facility within the DHB hospital.

DHBNZ will continue to support the maintenance of the national bleeding disorder database. DHBNZ will contract with HFNZ to support activities that HFNZ provide for DHBNZ and will contribute towards the maintenance of the haemophilia outreach service.

Regular meetings should be convened between NHMG and DHBs so as to monitor contract activity and discuss evolving issues concerning haemophilia care.

13. Purchase of coagulation factor concentrates

It is recommended that regular discussions take place between NHMG and PHARMAC to ensure that the purchase of coagulation factor concentrates meets the needs of patients.

There have been recurrent problems concerning the ability of manufacturers to provide a continuous supply of coagulation factor concentrates that meets demands. Patient care has been compromised as a result of past product shortages. As these shortages are often unpredictable, contractual processes should therefore be flexible enough to address these potential supply problems. In particular, the use of a single supplier is no longer acceptable to clinicians or patients.

14. Implementation of the specifications

Implementation of this specification will be monitored by the NHMG.

15. Date of issue

1st May 2014.

16. Recommended review

This specification is written at a time when haemophilia treatment is changing radically. For these reasons, the document should be reviewed in 2 years.

17. Definitions

Prophylaxis. Regular intravenous treatment with factor concentrate given to prevent bleeding. In haemophilia A this is typically administered three times a week and in haemophilia B, twice a week.

Inhibitor. An antibody produced by a person with a congenital coagulation factor deficiency that is directed against the factor that is deficient in their condition. Neutralising inhibitors reduce the effectiveness of exogenous factor replacement therapy

Immune tolerisation. The regular administration of high doses of factor VIII or IX over an extended period that eventually may lead to the patient being tolerant of the injected coagulation factor and the disappearance of the inhibitor, allowing the patient to be treated with factor VIII or IX.

18. References

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19. Appendices

Appendix 1. Membership of the New Zealand Haemophilia Treaters' Group

Membership of the New Zealand Haemophilia Treaters' Group (NZHTG) is limited to health professionals working in Haemophilia Treating Centres in New Zealand. This includes all medical staff with an interest in haemophilia management and all haemophilia nurses together with the national haemophilia physiotherapy specialist, and is supported by a secretary.

<u>Auckland</u> Dr Paul Ockelford Dr Laura Young Dr Nicola Eady Dr Lochie Teague Dr Nyree Cole Dr Peter Brad beer Mary Brassier (Haemophilia CNS) Karen Slavin (Haemophilia CNS)	<u>Wellington</u> Dr Julia Phillips Dr Huib Buyck Brian (BJ) Ramsay (Haemophilia CNS) Helen Dixon (Physiotherapist)
<u>Waikato</u> Dr Julie-Anne Bell Maureen Hayes (Haemophilia CNS)	<u>Christchurch</u> Dr Mark Smith Dr Siobhan Cross Kathy Fawcett (Haemophilia CNS) Lee Townsend (Physiotherapist)
<u>Palmerston North</u> Dr Paul Harper Daryl Pollock (Haemophilia CNS)	<u>Dunedin</u> Dr Hilda Mangos Amy Suddaby (Haemophilia CNS)

Appendix 2. Formal levels of published evidence.

Grade A

(Evidence levels Ia,Ib) Requires at least one randomised controlled trial as part of the body of literature of overall good quality and consistency addressing the specific recommendation.

Grade B

(Evidence levels IIa,IIb,IIc) Requires availability of well conducted clinical studies but no randomised controlled trials on the topic of the recommendation

Grade C

(Evidence level IV) Requires evidence from expert committee reports or opinions and/or clinical experience of respected authorities; indicates absence of directly applicable studies of good quality

Ia Meta analysis of randomised controlled trials

Ib At least one randomised controlled trial

IIa At least one well designed study without randomisation

IIb At least one well designed quasi-experimental Study

III Well designed non-experimental descriptive studies

IV Expert committee reports or opinions and/or clinical experience of respected authorities

Appendix 3. Specialist coagulation laboratory tests required by haemophilia treatment centres

APTT

Prothrombin time

Fibrinogen

Factor assays

- II
- V
- VII
- VIII
- IX
- XI

Inhibitor assays

Von Willebrand's assays

- Von Willebrand's antigen
- Ristocetin cofactor
- Collagen binding assay
- FVIII binding assay
- Von Willebrand's multimers

Platelet aggregometry

Testing for storage pool disease

Appendix 4. Data set required for NZ National Haemophilia Database

Registration data:

- Name
- NHI
- Sex
- Date of birth
- Basal level of factor VIII/IX
- Treatment centre

Follow-up data:

- Clinical status (free text e.g. target joints, surgery pseudotumour)
- Inhibitor status
- Dose of prophylaxis units/kg x per week
- Current treatment, including home therapy
- Product type

Appendix 4. National audit framework

Clinical

Treatment data, including number of patients:

- With severe haemophilia
- On home therapy
- On prophylaxis
- With inhibitors

On-call arrangements

Availability of support services, including paediatrics, orthopaedics, dental services

Arrangement for access to specialised HIV and Hepatitis care

Access to genetic services

Inspection of facilities

Review of staffing levels

Review of previous internal clinical audits

Arrangements for education and training

Clinical governance

Patient satisfaction

Laboratory

CPA accreditation

Review of NEQAS results

Review of internal audit

Availability of specialised coagulation assays during routine and emergency hours

Data handling

Coagulation factor concentrate stock control and handling

Annual returns to centralised database

Home therapy returns

Communication with other haemophilia centres and general practitioners

Protocols

Treatment delivery

Prophylaxis

Home therapy

On-call arrangements

Closing the audit loop

Issues arising from previous external audits

Publication and communication of results to interested parties

Appendix 5: Quality Improvement Plan for NZ Haemophilia Service

Objectives:

1. To develop and maintain a culture of quality and quality improvement in routine practice throughout the national bleeding disorder service
2. To perform annual formal quality assurance activities and to report the results to DHBs through the annual report of NHMG to DHB CEOs.
3. To adapt, over time, the quality assurance measures to match the changing needs of the service.

Quality Standards:

1. NZ National Haemophilia Service Specifications
2. NZ National Haemophilia Management Guidelines
3. World Federation of Haemophilia Guidelines

Quality assurance activities:

1. Perform national annual service audit
2. Assure NHMG that IANZ accreditation of diagnostic laboratories has been maintained
3. Participation in EUHASS international surveillance programme for adverse events

Quality measures for annual audit:

These will address:

- Accommodation and staffing for the provision of comprehensive care
- Cost of treatment products
- Clinical outcomes

A list of measures that are currently appropriate are attached. With time the specific measures may change as the needs and priorities of the service change.

Responsibilities:

NHMG

- To hold quarterly meetings with appropriate stakeholders as outlined in the NHMG terms of reference
- To ensure that the NZTG maintains quality activities outlined below and to review annual audit in the context of advice from NZTG
- To review areas of the service that NZTG have identified as being in need of improvement and agree with NZTG the actions required to address these
- To provide an annual report to DHB CEOs on the quality activities and the outcomes of the annual quality audit.
- To review impact of agreed quality improvement actions with NZTG

NZTG

- To hold quarterly meetings and report on these to NHMG

- Review treatment standards to ensure that these are consistent with best current practice
- Review quality standards to ensure that these remain appropriate
- To review the results of each annual audit, identify areas that require improvement and recommend measures to address any deficiencies that are identified to NHMG
- To implement quality improvement actions that have been agreed with NHMG
- To measure the impact of agreed quality improvement actions and report to NZHMG

HTCs

- To provide a service that meets agreed quality standards
- To send representatives to quarterly national haemophilia treaters meetings, and NHMG meetings as required.
- To collect and provide relevant quality data annually on request from NHMG in a timely manner
- To contribute to external quality assurance schemes as deemed appropriate by NHMG eg EUHASS adverse event reporting.

DHBs

- To ensure that adequate funding, accommodation and staffing are available for the provision of the services outlined in the service specifications
- To review the annual report on quality activities provided to them by NHMG

Haemophilia outcome measures

DATA SET:

a. For NZ service

1. Number of patients registered with each disease category, including symptomatic and asymptomatic carriers
2. Cost of products used

b. For each HTC

1. Accommodation and staffing

- Number of patients with severe haemophilia
- Dedicated haemophilia centre or not
- Total haematologist FTE allocated to haemophilia
- Haemophilia nurse FTE
- Haemophilia physiotherapy FTE
- Access to other comprehensive care components:- diagnostic laboratory; dental service; paediatrician; orthopaedic surgeon; rheumatologist; hepatologist; ID physician; geneticist; psychologist; social worker; obstetrics and gynaecology.

b. For each person with haemophilia:

1. Diagnosis and severity
2. Genetic analysis done/not done for family mutation
3. Age

4. BMI

5. Product use

- Total of each product

It is beneficial to Provide Break down of Product use by-

- Surgical
- Tolerisation
- Prophylaxis
- Other = bleed treatment

6. Bleed reporting

- Number of reported bleeds
- Time to reporting and % of these reported to HTC within 24 hrs.
- Time to physiotherapy assessment and % of these seen/advised within 24 hrs.

7. Work and school

- Full or part time education, full or part-time work, unemployed, retired.
- For those in education – time off education/school for haemophilia related reasons
- For those in work – time off work for haemophilia related reasons

8. Joint score

9. Hepatitis C

- Active hepatitis C – yes/no/not known
- Liver fibrosis as a consequence of hepatitis C – yes/no/not known
- If active hepatitis C or liver fibrosis currently under hepatology service – yes/no/not known

10. Quality of life assessment (HRQOL)

Analysis:

1. Summary of total registered population, including

- Number registered with each condition
- Estimate of undiagnosed patients from published epidemiological data
- Estimate of undiagnosed carriers from published epidemiological data.

2. Cost of national product use.

- Cost of treatment for each diagnostic group

3. For haemophilia population

- Age distribution of people with severe and non-severe haemophilia
- Number and proportion of obese people with severe and non-severe haemophilia
- Costs of surgical, tolerisation, prophylaxis and bleed treatments
- Ratio of reported bleeds to product use for bleeds
- Ratio of bleeds reported within 24 hrs. to total reported bleeds
- Time from reporting to physiotherapy assessment
- % of adults of working age in part time or full time education, part time or full time work.
- Range and median number of days off education/work in school and working age ranges
- Range, median, distribution and population trends in joint scores

- Range, median, distribution and population trends in HR-QOL parameters.
- Number of people with active hepatitis C
- Number of people with hepatitis C related liver fibrosis
- Proportion of people with active hepatitis C or liver fibrosis that are under a specialist hepatology service

Data Collection for points 5,6 and 7 are highly reliant on Patient provision of detailed treatment diaries. The promotion and assessment of treatment diaries is an area that HTCs are actively trying to address and improve. As this data input improves the data of outcome measures will also improve.