Clinical research brings improved therapies to market and provides an opportunity for patients to contribute to advance care and treatment. Clinical research may also improve overall understanding of bleeding and clotting disorders, increase knowledge of genetics, and provide ongoing safety information of therapy. Clinical research studies may offer patients and payors substantial treatment and genetic testing-related cost savings.

The IHTC has a long standing history of leadership in clinical research. The IHTC performed the first in the world human infusion of the following products:

1. genetically engineered factor IX concentrate
2. long-acting genetically engineered immunoglobulin fused factor IX concentrate
3. genetically engineered von Willebrand factor concentrate
4. genetically engineered bio-similar factor IX concentrate

The IHTC is a leader in clinical research with 45 currently active studies available to eligible patients. The IHTC independently evaluates the need for a specific study weighing how it may impact future patient care; above all the safety of the project is critically evaluated. There are a variety of different clinical research categories including pharmaceutical, investigator initiated, quality of life analyses and studies with national funding including the Centers for Disease Control and Prevention (CDC) or National Institute of Health (NIH).

The IHTC research coordinators connect patients to available studies and provide ongoing follow-up and coordination for the duration of the study for those enrolled. Below is a list of some of the important current studies related to the bleeding disorder community.

**Studies Open to All**

**IHTC Biorepository** was established as part of the IHTC commitment to research. The Biorepository is a collection of biological samples such as plasma and DNA voluntarily provided by patients and family members. These de-identified samples are used to advance the management and outcomes of bleeding and clotting disorders.

**ATHNdataset** is a national HTC and ATHN project to monitor trends, address unanswered questions, gain a better understanding of bleeding and clotting disorders, inhibitors, and treatment, develop cost effective care, and monitor the safety of therapies.

**My Life Our Future** is an initiative from NHF, ATHN, Puget Sound Blood Center and Biogen Idec. The aim is to genetically test individuals with factor VIII or IX deficiency in the US. Genotyping is free. In the future they will offer carrier testing as well.

**Cardiovascular Disease in Hemophilia** is a study to determine the history of stroke, prevalence of heart disease and symptoms of atherosclerosis in men aged 54-73 years with severe or moderate hemophilia. The study seeks to understand the similarities and differences in risk factors for heart disease, stroke, and atherosclerosis between men with hemophilia and a group of US men of similar age without hemophilia.

**The CDC Public health Surveillance Project/HTC Population Profile** will delineate the demographics, diagnoses and health service utilization of a population of patients that receive care through federally funded hemophilia treatment centers across the US. The study will assess, by comparison across years, what proportion of the annual HTC census is comprised of “new” or “infrequent” service users versus those who use services routinely or repeatedly.
Hemophilia A Studies

**Long Acting Products** have the potential to improve treatment due to less frequent infusions, and improve compliance and quality of life. The IHTC has one long-acting factor VIII fusion product study open for enrollment.

**Development of Inhibitors in Mild Hemophilia during Surgical Procedures** compares two currently established methods of administering factor VIII concentrate during procedures to determine their effect on subsequent inhibitor development. The study evaluates the immune system to investigate markers of inhibitor development to help predict or prevent inhibitor formation.

**Comparison of Secondary Prophylaxis Versus Episodic (On Demand) Treatment** in adults evaluates the number of bleeding events that occur yearly and their consequences in severe hemophilia A individuals who were not treated with prophylaxis prior to study entry. This study helps to establish whether prophylaxis in adults previously treated with on-demand therapy can prevent or reduce bleeding events, and improve joint preservation and other aspects such as cost and quality of life.

**Hemophilia Inhibitor PUP Study (HIPS)** evaluates immune factors related to inhibitor development in children. There are a variety of factors that impact development of an inhibitor including the individual immune system, environmental factors, and the genetic defect. This study evaluates the link between the immune system and inhibitors. This information could be used in the future to predict and/or prevent inhibitors.

**Hemophilia Inhibitor Genetics Study (HIGS)** identifies genetic factors associated with inhibitor formation in patients with hemophilia A. Mutations within the factor VIII gene are known to affect inhibitor development, a serious obstacle in hemophilia. This study focuses on the relationship between genetic factors and inhibitors and hopes to predict and/or prevent inhibitor development in the future.

Hemophilia B Studies

**Long Acting Products** have the potential to improve treatment due to less frequent infusions, and improve compliance and quality of life. The IHTC has two long-acting factor IX infusion products with studies open to enrollment.

**Hemophilia Costs and Impact of Disease Study (HUGS)** documents the financial and psychological cost of Hemophilia B. This study examines joint disease, quality of life, and financial impact on patients. The study combines patient interviews and chart reviews for individuals in four states.

Von Willebrand Disease

**The Composite Score Test** has been shown to be highly predictive of VWD in children. The study validates how well the composite test performs in a group of children undergoing VWD testing. Scoring questions based on bleeding symptoms, anemia, family history and early childhood bleeding may predict the likelihood of diagnosis and are compared to the standard clinical and laboratory testing for VWD.

**PPG-VWD Study** links the relationship between changes causing VWD and the clinical impact on the diagnosis and management of bleeding disorders in families diagnosed with VWD. The study uses bleeding symptoms, standard laboratory tests, and genetic testing to determine if other genes or proteins contribute to bleeding symptoms or abnormal VWD testing. Definitive diagnosis impacts how to deliver treatment to prevent or minimize bleeding during surgery or severe trauma, thus testing family members is important.

Investigator Initiated Projects

**Female Carriers of Hemophilia B** is a data collection study to explore the relationship of “modifier” genes and environmental factors in the expression of factor IX to better understand the causes of variation in levels. Information regarding medical and bleeding history is obtained, in addition to blood levels, to determine factor IX levels and genetic analysis.

**Intracranial Hemorrhage (ICH) in Children** with severe hemophilia is a collaborative study with Malmo University in Sweden. This study strives to determine whether prophylaxis treatment versus on-demand therapy can prevent or reduce the occurrence of intracranial hemorrhage-related quality of life aspects.