Hemophilia Market Assessment Study- MR Methodology

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TO WHOMSOEVER MAY CONCERN

This is to certify that SAYM ANSARI student of Post Graduate Diploma in Pharmaceutical Management (PGDPM) from Institute of Health Management Research; Jaipur has undergone internship training at INSTITUTE OF HEALTH MANAGEMENT RESEARCH, JAIPUR from 3rd FEBRUARY, 2014 to 30 APRIL, 2014.

The Candidate has successfully carried out the study designated to him during internship training and his approach to the study has been sincere, scientific and analytical.
The Internship is in fulfillment of the course requirements.
I wish him all success in all his future endeavors.

Dean, Academics and Student Affairs
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CERTIFICATE BY SCHOLAR

This is to certify that the dissertation titled "HEMOPHILIA MARKET ASSESSMENT STUDY" submitted by SAYM ANSARI Enrollment No.194 under the supervision of Dr. SANDEEP NARULA for award of Postgraduate Diploma in Pharmaceutical Management of the Institute carried out during the period from 2012 to 2014 embodies my original work and has not formed the basis for the award of any degree, diploma associate ship, fellowship, titles in this or any other Institute or other similar institution of higher learning.

Signature

Executive Summary

Hemophilia is a rare bleeding disorder which affects people of all sections of the society. The disease is lifelong, incurable in nature and very expensive to manage in terms of medicationand care. Recurrent and prolonged bleeding in joints and muscles can lead to permanent disability. Bleeding from the sensitive organs can lead even to death.

People with hemophilia not only suffer due to bleeding & pain but also face different kinds of challenges like getting proper treatment on time, adequate medicines (AHF) which is also very expensive, lack of proper diagnosis, financial crisis, psycho-social issues, education & building career etc.

From last 29 years, the Hemophilia Federation (India) has been addressing these issues through implementation of different projects and programmes for the welfare of more than 14,000 hemophiliacs of our country.

Established in 1983, HFI is run by Persons with Hemophilia themselves, with the help from medical fraternity through a network of 74 chapters spread over the country. We represent India as National Member Organization at the World Federation of Hemophilia based in Canada. We also work in close collaboration with World Health Organization (WHO) and National Aids Control Organization (NACO).

Introduction

Haemophilia is a lifelong bleeding disorder that prevents blood from clotting properly. People with hemophilia do not have enough clotting factor, a protein in blood that controls bleeding. The severity of a person's haemophila depends on the amount of clotting factor that is missing.

A person with hemophilia does not bleed faster than anyone else, but bleeding may last longer. The main danger is uncontrolled internal bleeding that starts spontaneously or results from injury. Bleeding into joints and muscles can cause stiffness, pain, severe joint damage, disability, and sometimes death.

Hemophilia usually is inherited. "Inherited" means that the disorder is passed from parents to children through genes.

People born with hemophilia have little or no clotting factor. Clotting factor is a protein needed for normal blood clotting. There are several types of clotting factors. These proteins work with platelets (PLATE-lets) to help the blood clot.

Platelets are small blood cell fragments that form in the bone marrow—a sponge-like tissue in the bones. Platelets play a major role in blood clotting. When blood vessels are injured, clotting factors help platelets stick together to plug cuts and breaks on the vessels and stop bleeding.

The two main types of hemophilia are A and B. If you have hemophilia A, you're missing or have low levels of clotting factor VIII (8). About 8 out of 10 people, who have hemophilia, have type A. If you have hemophilia B, you're missing or have low levels of clotting factor IX (9).

Hemophilia can be mild, moderate, or severe, depending on how much clotting factor is in your blood. About 7 out of 10 people who have hemophilia A have the severe form of the disorder.

People who don't have hemophilia have a factor VIII activity of 100 percent. People who have severe hemophilia A have a factor VIII activity of less than
1 percent.

Haemophilic arthropathy is characterized by chronic proliferative synovitis and cartilage destruction. If an intra-articular bleed is not drained early, it may cause apoptosis of chondrocytes and affect the synthesis of proteoglycans. The hypertrophied and fragile synovial lining while attempting to eliminate excessive blood may be more likely to easily rebleed, leading to a vicious cycle of hemarthrosis-synovitis-hemarthrosis. In addition, iron deposition in the synovial may induce an inflammatory response activating the immune system and stimulating angiogenesis, resulting in cartilage and bone destruction.

LITERATURE REVIEW

In India, incidence of Haemophilia is about 1 in 10,000 male births.Around 1/3rd of the new cases are caused by genetic mutation of the gene in mother or child, with no previous history of Haemophilia in the family.The diagnosis of the disorder is either determined by presentation of the symptoms like prolonged bleeding, unexplained bleeding and so on, or on the basis of previous family history.There is no predominant age group which is affected by Haemophilia. It is usually inherited since birth and remains with the patient life long. Factor utilisation in India is estimated to be 35%-40%. Undiagnosed patients, spontaneous or sudden bleeding caused by an injury, non availability of the treatment centres and high cost of therapy are the major challenges in the management of the disorder.

Haemophilia A (clotting factor VIII deficiency) is the most common form of the disorder, present in about 1 in 5,000–10,000 male births. Haemophilia B (factor IX deficiency) occurs in around 1 in about 20,000–34,000 male births.

Like most recessive sex-linked, X chromosome disorders, haemophilia is more likely to occur in males than females. This is because females have two X chromosomes while males have only one, so the defective gene is guaranteed to manifest in any male who carries it. Because females have two X chromosomes and haemophilia is rare, the chance of a female having two defective copies of the gene is very remote, so females are almost exclusively asymptomatic carriers of the disorder. Female carriers can inherit the defective gene from either their mother or father, or it may be a new mutation. Although it is not impossible for a female to have haemophilia, it is unusual: a female with haemophilia A or B would have to be the daughter of both a male haemophiliac and a female carrier, while the non-sex-linked haemophilia C due to coagulant factor XI deficiency, which can affect either sex, is more common in Jews of Ashkenazi (east European) descent but rare in other population groups.

Haemophilia lowers blood plasma clotting factor levels of the coagulation factors needed for a normal clotting process. Thus when a blood vessel is injured, a temporary scab does form, but the missing coagulation factors prevent fibrin formation, which is necessary to maintain the blood clot. A haemophiliac does not bleed more intensely than a person without it, but can bleed for a much longer time. In severe haemophiliacs even a minor injury can result in blood loss lasting days or weeks, or even never healing completely. In areas such as the brain or inside joints, this can be fatal or permanently debilitating.

Signs and Symptoms

Characteristic symptoms vary with severity. In general symptoms are internal or external bleeding episodes, which are called "bleeds". Patients with more severe haemophilia suffer more severe and more frequent bleeds, while patients with mild haemophilia usually suffer more minor symptoms except after surgery or serious trauma. Moderate haemophiliacs have variable symptoms which manifest along a spectrum between severe and mild forms.

In both haemophilia A and B, there is spontaneous bleeding but a normal bleeding time, normal prothrombin time, normal thrombin time, but prolonged partial thromboplastin time.Internal bleeding is common in people with severe haemophilia and some individuals with moderate haemophilia. The most characteristic type of internal bleed is a joint bleed where blood enters into the joint spaces. This is most common with severe haemophiliacs and can occur spontaneously (without evident trauma). If not treated promptly, joint bleeds can lead to permanent joint damage and disfigurement. Bleeding into soft tissues such as muscles and subcutaneous tissues is less severe but can lead to damage and requires treatment.

Children with mild to moderate haemophilia may not have any signs or symptoms at birth especially if they do not undergo circumcision. Their first symptoms are often frequent and large bruises and haematomas from frequent bumps and falls as they learn to walk. Swelling and bruising from bleeding in the joints, soft tissue, and muscles may also occur. Children with mild haemophilia may not have noticeable symptoms for many years. Often, the first sign in very mild haemophiliacs is heavy bleeding from a dental procedure, an accident, or surgery. Females who are carriers usually have enough clotting factors from their one normal gene to prevent serious bleeding problems, though some may present as mild haemophiliacs.

Complications

Severe complications are much more common in severe and moderate haemophiliacs. Complications may be both directly from the disease or from its treatment:

- **Deep internal bleeding**, e.g. deep-muscle bleeding, leading to swelling, numbness or pain of a limb.
- **Joint damage** from haemarthrosis (haemophilic arthropathy), potentially with severe pain, disfigurement, and even destruction of the joint and development of debilitatingarthritis.
- **Transfusion transmitted infection** from blood transfusions that are given as treatment.

- **Adverse reactions** to clotting factor treatment, including the development of an immune inhibitor which renders factor replacement less effective.
- **Intracranial haemorrhage** is a serious medical emergency caused by the buildup of pressure inside the skull. It can cause disorientation, nausea, loss of consciousness,brain damage, and death.

Life expectancy

Like most aspects of the disorder, life expectancy varies with severity and adequate treatment. People with severe haemophilia who don't receive adequate, modern treatment have greatly shortened lifespan and often do not reach maturity. Prior to the 1960s when effective treatment became available, average life expectancy was only 11 years. By the 1980s the life span of the average haemophiliac receiving appropriate treatment was 50–60 years. Today with appropriate treatment, males with haemophilia typically have a near normal quality of life with an average lifespan approximately 10 years shorter than an unaffected male.[]

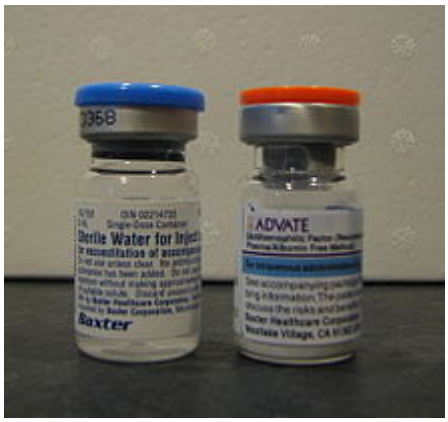
Since the 1980s the primary leading cause of death of people with severe haemophilia has shifted from haemorrhage to HIV/AIDS acquired through treatment with contaminated blood products.[] The second leading cause of death related to severe haemophilia complications is intracranial haemorrhage which today accounts for one third of all deaths of patients with haemophilia. Two other major causes of death include hepatitis infections causing cirrhosis and obstruction of air or blood flow due to soft tissue haemorrhage.

Causes

- **Haemophilia A** is a recessive X-linked genetic disorder involving a lack of functional clotting Factor VIII and represents 80% of haemophilia cases.
- **Haemophilia B** is a recessive X-linked genetic disorder involving a lack of functional clotting Factor IX. It comprises approximately 20% of haemophilia cases.
- **Haemophilia C** is an autosomal genetic disorder (i.e. *not* X-linked) involving a lack of functional clotting Factor XI. Haemophilia C is not completely recessive, as heterozygousindividuals also show increased bleeding.

Management

Commercially produced factor concentrates such as 'Advate', a recombinant factor VIII, come as a white powder in a vial which must be mixed with sterile water prior to intravenous injection.



through there is no cure for haemophilia, it can be controlled with regular infusions of the deficient clotting factor, i.e. factor VIII in haemophilia A or factor IX in haemophilia B. Factor replacement can be either isolated from human blood serum, recombinant, or a combination of the two. Some haemophiliacs develop antibodies (inhibitors) against the replacement factors given to them, so the amount of the factor has to be increased or non-human replacement products must be given, such as porcine factor VIII.

In early 2008, the US Food and Drug Administration (FDA) approved Xyntha (Wyeth) anti-haemophilic factor, genetically engineered from the genes of Chinese hamster ovary cells. Since 1993 (Dr. Mary Nugent) recombinant factor products (which are typically cultured in Chinese hamster ovary (CHO) tissue culture cells and involve little, if any human plasma products) have been available and have been widely used in wealthier western countries. While recombinant clotting factor products offer higher purity and safety, they are, like concentrate, extremely expensive, and not generally available in the developing world. In many cases, factor products of any sort are difficult to obtain in developing countries.

In Western countries, common standards of care fall into one of two categories: prophylaxis or on-demand. Prophylaxis involves the infusion of clotting factor on a regular schedule in order to keep clotting levels sufficiently high to prevent spontaneous bleeding episodes. On-demand treatment involves treating bleeding episodes once they arise.

In 2007, a clinical trial was published in the *New England Journal of Medicine* comparing on-demand treatment of boys (< 30 months) with haemophilia A with prophylactic

treatment (infusions of 25 IU/kg body weight of Factor VIII every other day) in respect to its effect on the prevention of joint-diseases.

Preventive exercises

- It is recommended that people affected with haemophilia do specific exercises to strengthen the joints, particularly the elbows, knees, and ankles.[20] Exercises include elements which increase flexibility, tone, and strength of muscles, increasing their ability to protect joints from damaging bleeds. These exercises are recommended after an internal bleed occurs and on a daily basis to strengthen the muscles and joints to prevent new bleeding problems. Many recommended exercises include standard sports warm-up and training exercises such as stretching of the calves, ankle circles, elbow flexions, and quadriceps sets.

Alternative medicine

- While not a replacement for traditional treatments, preliminary scientific studies indicate that hypnosis and self-hypnosis may be effective at reducing bleeds and the severity of bleeds and thus the frequency of factor treatment. Herbs which strengthen blood vessels and act as astringents may benefit patients with haemophilia, however there are no peer reviewed scientific studies to support these claims.

Contraindications

- Anticoagulants such as Heparin and Warfarin are contraindicated for people with haemophilia as these can aggravate clotting difficulties. Also contraindicated are those drugs which have "blood thinning" side effects. For instance, medicines which contain aspirin, ibuprofen, or naproxen sodium should not be taken because they are well known to have the side effect of prolonged bleeding.

- Also contraindicated are activities with a high likelihood of trauma, such as motorcycling and skateboarding. Popular sports with very high rates of physical contact and injuries such as American football, hockey, boxing, wrestling, and rugby should be avoided by people with haemophilia.[25][26] Other active sports like soccer, baseball, and basketball also have a high rate of injuries, but have overall less contact and should be undertaken cautiously and only in consultation with a doctor.

RATIONALE

There are numerous different mutations which cause each type of haemophilia. It is estimated that there are around 125,000 patients with Haemophilia, out of which only 18,000 are diagnosed and registered patients. Haemophilia Federation of India maintains the national registry for the Haemophilia patients. This registry is comprehensive and consists upto 98% of the diagnosed patients in India

Due to differences in changes to the genes involved, patients with haemophilia often have some level of active clotting factor. Individuals with less than 1% active factor are classified as having severe haemophilia, those with 1-5% active factor have moderate haemophilia, and those with mild haemophilia have between 5-40% of normal levels of active clotting factor.

The development of hemophilic arthropathy is directly linked to the number of joint bleeding episodes. Among 378 patients enrolled in the landmark Orthopaedic Outcome Study, published in 1994, Pettersson radiologic scores (a measure of joint status) increased by 1 point for every 40 joint bleeds. A subsequent evaluation of 117 patients with severe hemophilia found that just 13 bleeds were necessary to cause a 1-point increase in the Pettersson score. However, even this lower number may be an overestimate, as plain film radiographs only visualize gross arthritic alterations. When children with hemophilia who had no obvious clinical signs of arthropathy underwent MRI, early changes in the soft tissues (e.g., synovium and cartilage) were apparent, indicating that incipient joint damage occurs after very few bleeding events.

Haemophilia Federation of India (HFI). Being a low volume high cost disease, in most developing countries haemophilia is utterly neglected. Though the WFH helped HFI in various ways they have been careful in keeping this vast country out of GAP (Global Alliance for Progress). The regulation to improve blood products and help given by National AIDS Control Programme of the Government of India has helped reducing the prevalence of HIV-1 infection among haemophilics from 13-14 to 6 per cent at present. Infact a few haemophilics who born after 1988, are now HIV positive. However, the same cannot be said about other two transfusion transmitted hepatitis viruses. About 10-14 per cent of PWH in India have hepatitis B infection and 24-30 per cent of them are positive for hepatitis C3. This is unlikely to reduce without universal use of factor concentrates for

haemophilia care. It is here that the Indian government needs to step in as financially it is not possible for any haemophilia patient to bear the burden of the cost of f factor concentrate required for his treatment.

OBJECTIVES

- Proportion split of various players in the hemophilia market (% shares not the market values as such).
- Kind of split between government and private players
- Total number of diagnosed and treated Hemophilia patients in India
- Distribution channel for hemophilia products
- Current usage of brands (% shares)
- Cost/ unit meaning procurement rates at which the hospitals are procuring these brands.

RESEARCH METHODOLOGY

Study Design:
The present study will be a cross sectional.

Study Area:
The respective study will be conducted in all four region of india.

Sampling and sample selection:
Channel Partners (n=20), Government and Private Institutions (n=40), Patients (n=10)

Data collection tool:
A semi structured interview will be used as a tool for the study. (Only for patients)

Data Management and Analysis
The collected data will be analyzed using EXCEL will be done and the respective results will be shown in form of frequency and percentage with the help of tables and graphs.

ETHICAL CONSIDERATION

Informed consent from the respondent will be obtained before starting interview. If anyone among the respondents refuses to became part of the data collection process they will not be forced by any means. Information given by the respondents will be kept confidential.

EPIDEMIOLOGY OF HAEMOPHILIA IN INDIA

"It is estimated that there are more than 1 lakh patients of Haemophilia in India but only 10%-15% of the patients are diagnosed and registered with HFI. In case of injury to undiagnosed Haemophilic patient, management and treatment of patient becomes very critical as clinicians are not able to diagnose the problem first hand and the treatment delays significantly" – ***Hemophilia Federation of India***

- Haemophilia is a lifelong bleeding disorder that prevents blood from clotting properly. The severity of a person's haemophilia depends on the amount of clotting factor that is missing
- In India, incidence of Haemophilia is about 1 in 10,000 male births
- Around 1/3rd of the new cases are caused by genetic mutation of the gene in mother or child, with no previous history of Haemophilia in the family
- The diagnosis of the disorder is either determined by presentation of the symptoms like prolonged bleeding, unexplained bleeding and so on, or on the basis of previous family history
- There is no predominant age group which is affected by Haemophilia. It is usually inherited since birth and remains with the patient, life long
- Factor utilisation in India is estimated to be 35%-40%
- Undiagnosed patients, spontaneous or sudden bleeding caused by an injury, non availability of the treatment centres and high cost of therapy are the major challenges in the management of the disorder
- It is estimated that there are around 125,000 patients with Haemophilia, out of which only 18,000 are diagnosed and registered patients
- Haemophilia Federation of India maintains the national registry for the Haemophilia patients. This registry is comprehensive and consists upto 98% of the diagnosed patients in India
- HFI has developed a robust web application as per the guidelines of advisory board and IT regulations
- All HFI chapters are equipped and trained for management of web application
- HFI has about 10 methods of collecting data in an efficient manner by being in contact with various state governments, organisations and NGOs.

India lacks a national policy on the prevention and control of genetic disorders. Although the hemoglobinopathies have received some attention, there is very little data on the epidemiology of other genetic disorders in India. Haemophilia, an inherited single gene disorder with an incidence of 1 per 10 000 births, manifests as spontaneous or traumainduced hemorrhagic episodes in patients, progressing to chronic disability and premature mortality in untreated patients or patients with sub-optimal treatment. Although the genetic basis of this disorder has been well studied in India, data on the number of

patients, trends of the disorder in India, social costs of the condition and opportunities and competencies for offering genetic counseling through a public health programme have not been reported. Our research using haemophilia demonstrates the need for prevention and for the provision of care for patients.

We have reported that India harbors the second highest number of global patients with bleeding disorders. The number of patients reported annually from India during the last five years, is more than those being reported from developed nations.

Trends of haemophilia in Maharashtra, India: India has the third highest global number of patients. We are analyzing twenty year data on trends of haemophilia in the state of Maharashtra, India. Using sixteen key variables, our analysis shows increasing annual case registrations, increase in the number of moderate and mild haemophilia cases, cases of other bleeding disorders, increasing registration of female patients, increasing numbers of patients from rural areas, earlier age at diagnosis—all indicative of improving diagnosis and increasing prevalence of the disorder. Our estimates suggest that there may be about 77 000 patients with haemophilia A and B in the country, even as there is no provision for prevention or treatment for these conditions.

DIAGNOSIS & TREATMENT CHANNEL

Diagnostic tests

Normally, when bleeding begins, a complex series of chemical events produces a "plug" to stop the bleeding; this plug is called a fibrin clot. If your doctor suspects that you have haemophilia, they will perform blood tests to examine how well your blood creates this clot. A lab mixes your blood with specific chemicals in a test tube to produce a fibrin clot. If such tests are abnormal, other blood tests are carried out to determine the amounts of factors VIII and IX in the blood. These tests help doctors diagnose the type of haemophilia and its severity.

Diagnosis of Hemophilia includes screening tests and clotting factor tests. Screening tests are blood tests that show if the blood is clotting properly. Clotting factor tests, also called factor assays, are required to diagnose a bleeding disorder

- Complete Blood Count (CBC) - *CBC and Hemoglobin count*
- Activated Partial Thromboplastin Time (APTT) Test - *Clotting factors (VIII, IX, XI and XII)*
- Prothrombin Time (PT) Test - C*lotting ability of factors*
- Fibrinogen Test - A*bility to form blood clot*
- Chorionic Villus Sampling (CVS) or Fetal blood sampling (18 or more weeks) – *If mother is a known carrier, testing can be done in prenatal stage*
- Inhibitor Assay – *Haemophilia patients to find out inhibitors development*

Treatment Options:

Haemophilia is treated by replacing the missing clotting factor in the blood. This is done by injecting a product that contains the needed factor into a vein. Due to the high cost of AHF, most patients in India may be required to take infusions of unsafe, wet blood products such as Fresh Frozen Plasma (FFP) or lyophilized cryoprecipitate. This necessity exposes patients to blood borne infections like HIV/AIDS and Hepatitis.

Treatments for haemophilia include:

- Receiving clotting factors
- Medication
- Treatment for joint bleeding and other problems associated with haemophilia

The treatments you need and their frequency depend on the type of haemophilia (A or B) and the severity of haemophilia. For instance, if you have mild haemophilia, you may need treatment only when you've been injured or in preparation for surgery. However, if you have severe haemophilia and bleed frequently, you may need regular treatment to prevent bleeding and protect your joints from deformity and disability.

Clotting factors for haemophilia

People with haemophilia receive the appropriate clotting factor (factor VIII or factor IX). The clotting factor is given intravenously (through a needle in your vein) to stop or prevent bleeding.

Medication for haemophilia A

A medication called desmopressin can temporarily increase the concentration of factor VIII in your blood. Desmopressin is usually given by injection.

Other health problems associated with haemophilia may need treatment. The most common include the following:

- Treating bleeding joints
- Monitoring physical activities

For bleeding joints, doctors recommend resting and icing the affected joint to decrease pain and swelling. As pain and swelling subsides, physiotherapy may help a person recover joint mobility and strength.

Monitoring physical activity may be necessary to prevent injury and internal bleeding. Your doctor will discuss the types of physical activities that are appropriate and what kinds of activities may be too dangerous. Your doctor's advice depends on the severity of haemophilia.

Of the total patient receiving factor concentrates almost 98% cases seek treatment on need basis, and a maximum of 1 % to 2% patients take prophylactic therapy, which is also determined by the socio economic status of the patient.

Treatment and out of pocket expenditure: Using a follow up study, we analyzed bleeding patterns, treatment and out of pocket expenditure on haemophilia treatment. The results showed that due to financial reasons, only one in four bleeding episodes were treated by families. Annualized bleeding rate was 10.8 for patients with severe hemophilia. If all bleeding episodes were to be treated, the monthly expenditure would range from 25 to 255 times the monthly income of families.

Disability in patients with haemophilia: Lack of treatment of haemophilia results in progressive disability. The consequence of lack of treatment was measured in a study that estimated the prevalence and risk factors of disability amongst patients attending three clinics in Western India and two clinics from Eastern India. Only nine of 148 patients were free of disability. The proportion of disability free patients in the 5–12, 13–24 and 25+ age groups were 14.3%, 4.4%, and 0% respectively.

Events: HFI organized and participated in several awareness and fund raising events. The major events organized were:

- Bangalore Hemophilia Walkathon-2013

- Mysore Hemophilia Walkathon-2013

- World Hemophilia Day Celebration

Participated in:

- Airtel Delhi Half Marathon-2013

- Ability Expo - 2013 organized by Technia Institute of

Rehabilitation Science and Research

Sources of Funds	Amount (in lacs)
Receipt Against AHF:	47196832
Corporate Funding, Projects (including FCRA) :	8773239
School Fund Raising:	1544925
Direct Marketing:	4866089
Others:	2337767.50

HFI Supporters and Collaborators:

- **NACO**
- **ONGC**
- **SAIL**
- **BHEL**
- **The Hans Foundation**
- **Give India**
- **VMWare**
- **Novo Nordisk**
- **Baxter India**
- **South India Agency**
- **Shiv Trading company**
- **Vimal Veneet**
- **Synergies**
- **Kalyani Motors**

SEVERITY OF HEMOPHILIA

Severity: The level of severity depends on the amount of clotting factor that is missing from a person's blood

- NORMAL

Around **50% - 150%** of the normal activity of clotting factor VIII (8) or IX (9) in the blood

- MILD HEMOPHILIA

Around 5% - 30% of normal clotting factor activity

- Might bleed for a long time after surgery or a very bad injury
- Might never have a bleeding problem
- Do not bleed often
- Do not bleed unless injured

- MODERATE HEMOPHILIA

Around 1% - 5% of normal clotting factor activity

- Might bleed for a long time after surgery, a bad injury, or dental work
- Might bleed about once a month
- Rarely bleed for no clear reason

- SEVERE HEMOPHILIA

Less than 1% of normal clotting factor activity

- Bleed often into the muscles or joints

- Might bleed one or two times per week

<u>Correlation of severity with International units per mL of whole blood :</u>

Level	Percentage of normal factor activity	Number of international units (IU) per millilitre (ml) of whole blood	% of Haemophilia patients
Normal range	50% - 150%	0.50 – 1.5 IU	-
Mild Haemophilia	5% - 30%	0.05 - 0.40 IU	35-40%
Moderate Haemophilia	1% - 5%	0.01 - 0.05 IU	20 %
Severe Haemophilia	less than 1%	less than 0.01 IU	40-45%

MARKET ANALYSIS

Clotting factors

- The overall market for clotting factors comprising of anti-haemophilic factors, blood plasma products and cryoprecipitate was estimated to be INR 1,480 million in year 2013.

- The market share for clotting factors was estimated to be around 52% in 2013 and is expected to grow with a rate of 7% by 2015 reaching up to INR 943 million.

- Clotting factors are primarily used for management of Hemophilia, moreover they also have utility in other conditions such as Surgeries, trauma, burns, oncology and so on.

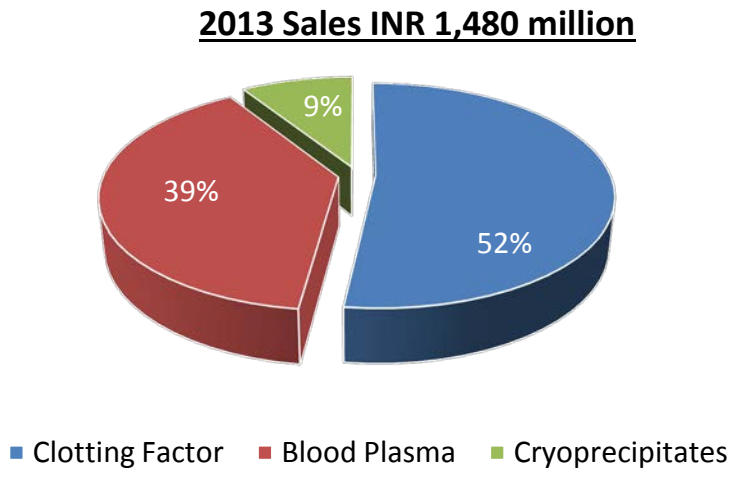
- **Key growth drivers for clotting factors market are as:**

- Increasing numbers of hemophilic A and B cases and certain surgeries.

- Increased life expectancy for hemophilia patients translates to longer usage period hence more consumption of clotting factors.

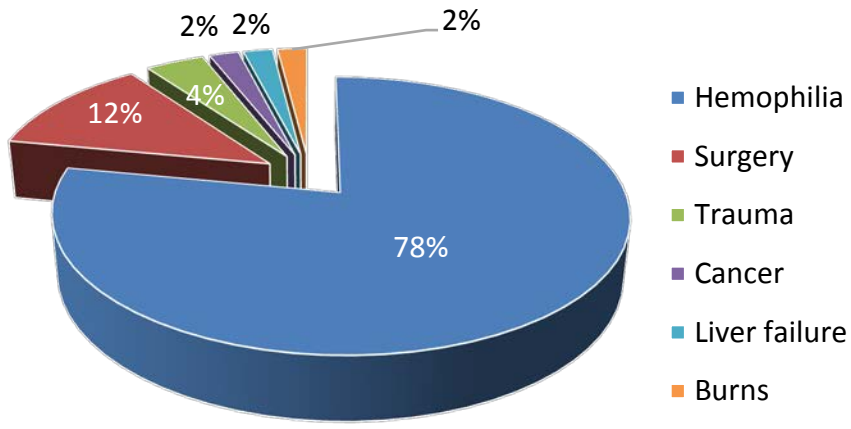
- Growing awareness of the condition hence an increasing number of new patients are registering for treatment at hospitals and other healthcare institutions.

- Rising income levels: Increasing expenditure is also responsible for higher utilization of recombinant and plasma derived coagulation factors.



- Indian scenario regarding the usage of clotting factor in different indications

Clotting factor usage

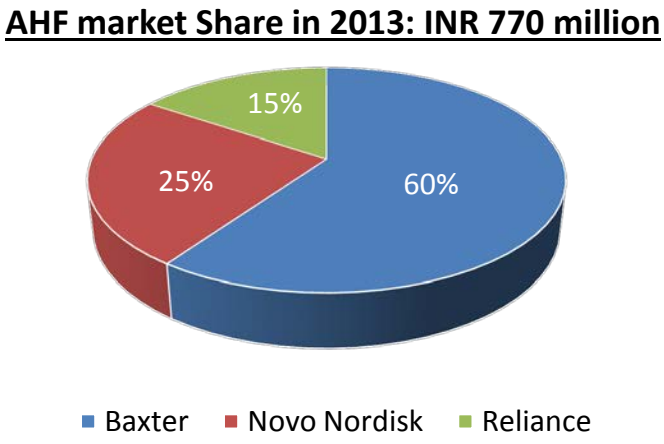


Proportion split of various players in the hemophilia market % shares not the market values

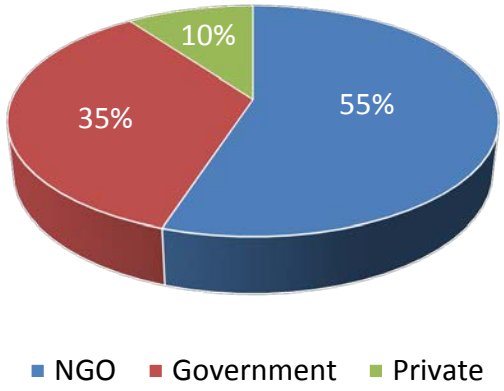
- In India, major companies which are active in Anti Hemophilia Factor segment are Baxter and Novo Nordisk
- Reliance is also present in the segment with a Factor VIII product "Hemorel". Hemorel is an imported product and have supply and shortage issues due to on and off import of the product.

Category	Brands	Factor	MRP in INR	Strength	Company	% Share in AHF sales
Non-recombinant	Hemophiliu m	Factor VIII	4,190	250 units	Baxter	40%
Non-recombinant	Hemonine	Factor IX	13,150	600 units		20%
Recombinan t	Feiba	Factor VIII inhibitor bypassin g activity	25,000	500 units		8%
Recombinan t	Recombinate	Non plasma factor VIII	29,500	1000 units		32%
Recombinan t	Novo Seven	Factor VII	86,900/43,40 0	2mg/1m g	Novo Nordisk	100%
Non-recombinant	Hemorel	Factor VIII	3,800	250 units	Reliance	100%

Indian AHF (anti haemophilia factor segment) scenario



AHF market by customers



Market Analysis in context with Prescriber and Cost

Percentage wise treatment of Hemophilia according to clinicians specialties

Hematologist	Pediatrician	Consulting Physician	General Surgeon
75%	20%	5%	1-2% (In case a patient undergoes surgery)

Cost comparison of Hemophilia factor treatment:

- Depending on the condition, haemophiliacs need factor 7, 8 or 9. Factor 8 is the most commonly needed AHF
- The cost of AHF varies from the type of injury and episode to episode. For instance, a simple injury may be treated by 2,000-2,500 units of AHF for a 50 kg body weight, but severe injury like intracranial injury can call for 30,000 units of AHF which will cost around INR 2 lakh

Factor	Per unit cost (In INR)	Average number of required units
Factor VIII	12	2,500
Factor IX	18	4,000
Factor VII	43,400	1-2 mg

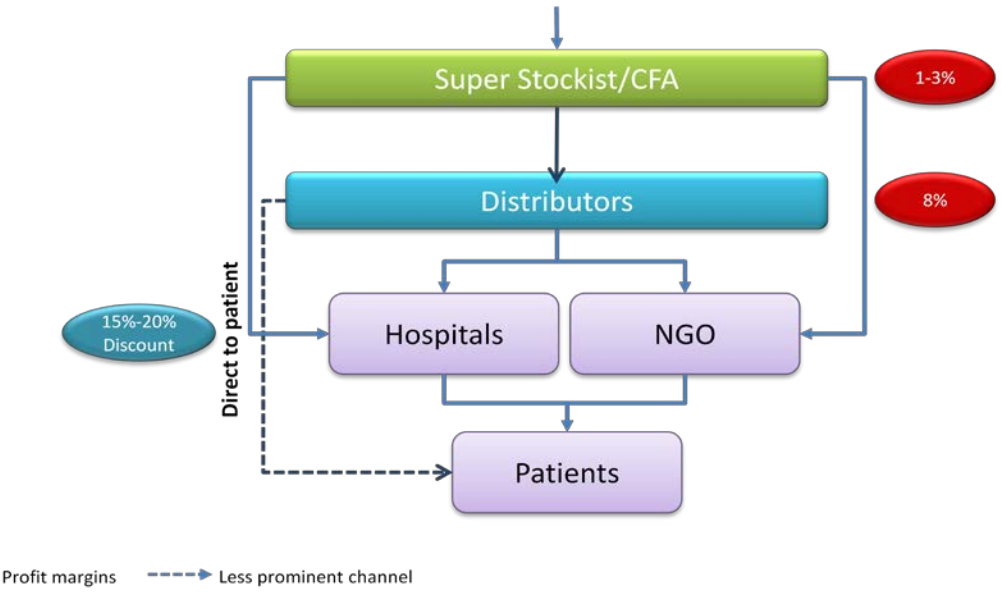
Income wise distribution of patients

- As Haemophilia is a low volume high value disease, irrespective of income slab, majority of the patients seek assistance from government/reimbursement organisations or HFI
- None of the insurance companies operating in India covers the expenses of the disorder due to high cost of treatment and its uncertain nature

Income Level*	% of patients
High Income (above INR 5 lac)	10%
Middle Income (INR 2-5 lac)	40-45%
Low Income (Upto INR 2 lac)	30%
BPL	15%

DISTRIBUTION CHANNEL

- All the available AHF products in India are imported
- AHF being very costly product, various NGO's and Hospitals are actively providing the therapy either free-of-cost or at affordable/subsidised prices to the patients . Hemophilia Society is one such example which procures AHF directly from the company at discounted prices and provides the same to the customer at economical rates or for free (depending on the patient affordability)
- Companies operating in the AHF segment provide drugs at a subsidized rates to the NGOs and health institutes

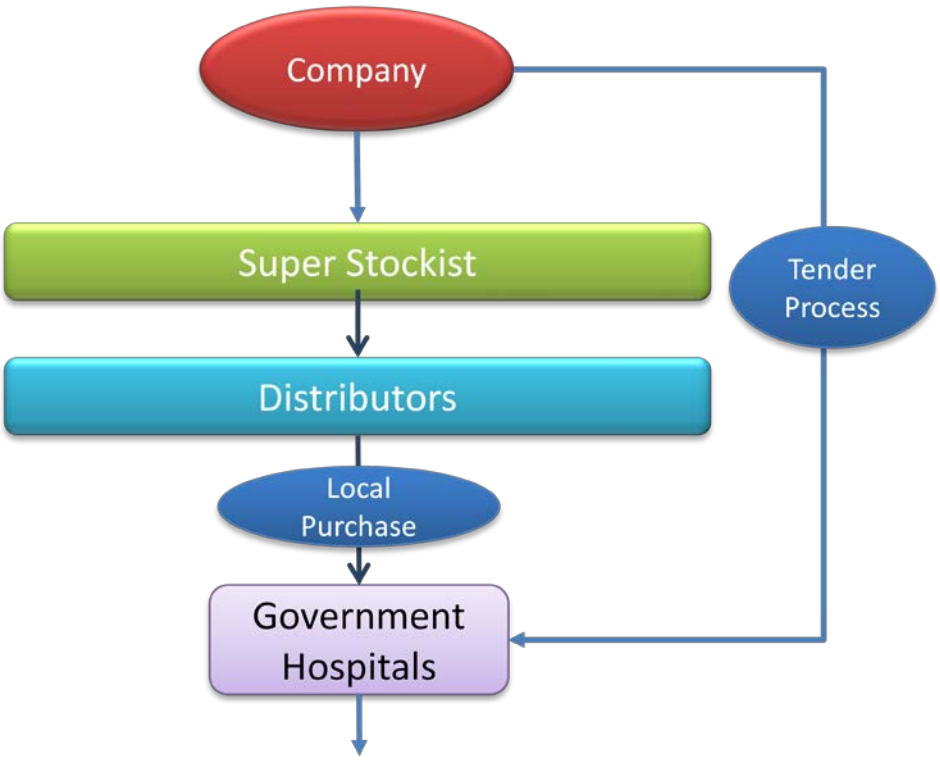


In case the patient purchase the AHF directly from dstributors, retailer/Hospital margins are passed on to patient as discounts. Baxter India provides a disacount of 22%-25% on MRP to patients and NGOs

Government distribution process:

- Certain NGOs and public hospitals are active in procurement and distribution of AHF product for instance Delhi government set up Hemophilia centers in three of its hospitals. Hemophilia Society of India and Hemophilia Federation of India are also actively working in providing support to patient population.
- Under government Hemophilia aid program, patients under BPL are provided with free medicines for the management of the disorder, whereas patients within income group of INR 2-5 lakh have to bear 30-50% of the product cost.

- In India, there are selected government institutes which offer treatment and management of Hemophilia for instance SGPGI, Lucknow; Lok Nayak Jai Prakash Hospital, Delhi and so on
- Karnataka government was the first in India to provide the free AHF drugs to BPL patients
- Government institutes procure the AHF usually through tender process and in case of supply issues, procure it through local purchase as well
- Liasioning agents are involved in the tender procurement of the target products
- Irregular supply and non availability of the AHF drugs are the major areas of concern in government organisations



Other Programmes

Communication

The communication dept has regularly published quarterly newsletter. During the year:

- F13,000 copies of Newsletter were published and distributed among our network.
- As north, east and west are Hindi speaking region, we have started Hindi version of the Newsletter keeping in mind their requirement.
- 6,000 copies of hemophilia educational materials were published and distributed to the general public including school students, medical fraternities, hemophilia patients and families.
- Annual Report for the year 2010-11 and Souvenir were published .
- New Brochure was designed, printed and distributed.
- We have improved the email communication within HFI network.
- Our website is being regularly updated.

LEADING HEMOPHILIA CENTERS

- **New Delhi**
- Lok Nayak Jai Prakash Hospital, Delhi Gate
- Deen Dayal Upadhyae Hospital, Hari Nagar
- Guru Teg Bahadur Hospital, Dilshad Garden

- **West Bengal**
- Kolkata Medica College

- **Bihar**
- Patna Medical College and Hospital (PMCH)

- **Karnataka**
- Bowring & Lady Corzon Hospital, Bengaluru
- Victoria Hospital, Bengaluru
- KC General Hospital, Bengaluru
- Wenlock Government Hospital, Manglore
- KR Hospital, Mysore
- District Hospital, Hassan
- District Hospial, Dharwad
- CG Hospital, Davangere

- **Tamil Nadu**
- For Pediatric patients: Institute for Child Health & Hospital for Children, Chennai
- General Hospital, Department of Hemophilia, Chennai

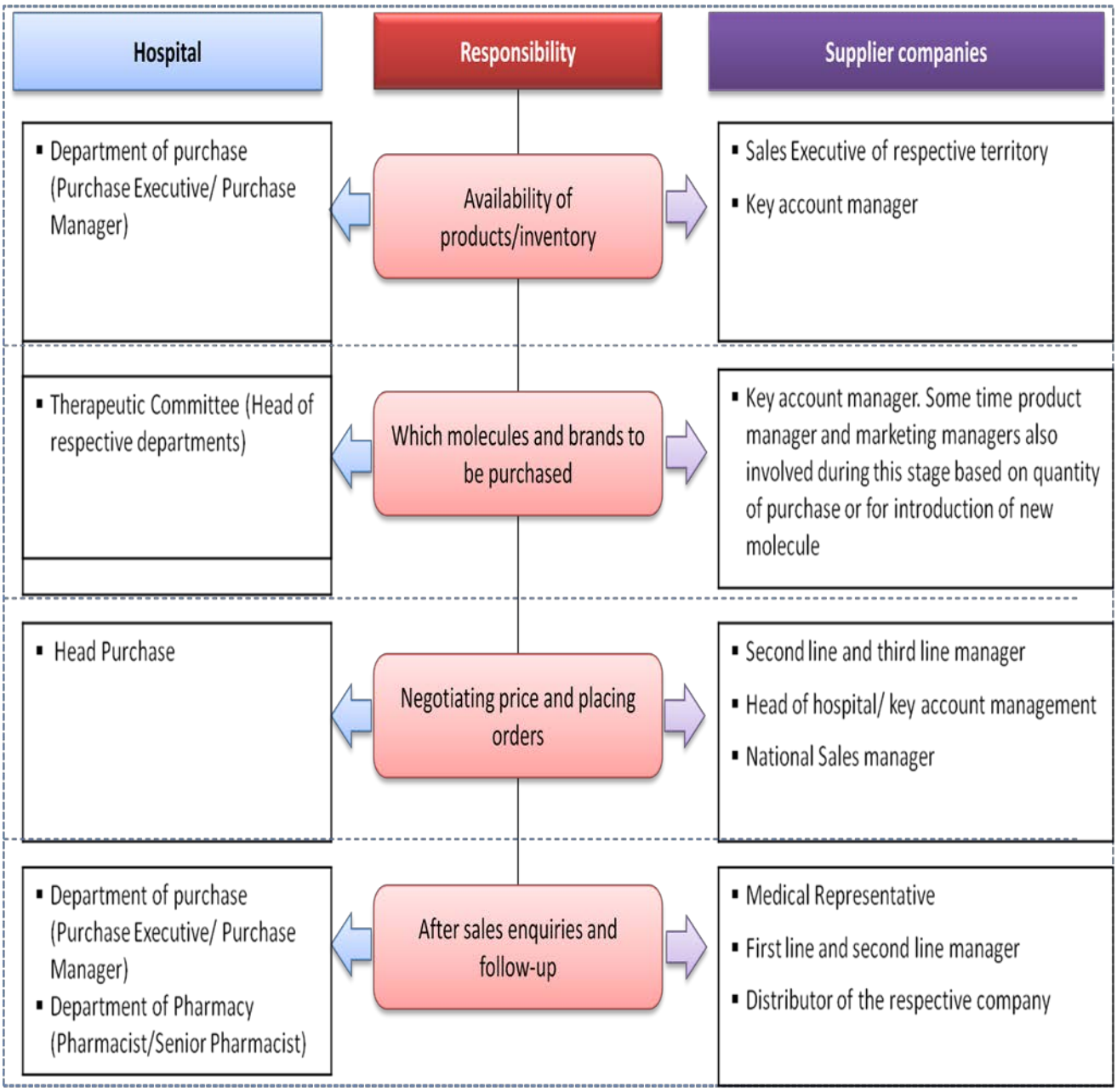
- **Puducherry**
- JIPMER Hospital
- Government Hospital

- **Uttar Pradesh**
- SGPGI and Medical College, Lucknow
- Medical College, Jhansi
- Medical College, Allahabad
- Medical College, Meerut
- Medical College, Kanpur
- **Jammu & Kashmir**
- Medical College, Jammu
- Medical College, Kashmir

MAIN FINDINGS

PRIVATE HOSPTIALS:

Following are the key points of contact between the supplying company and the hospital during the procurement process



GOVERNMENT HOSPTIALS:

Calling upon tenders

- Purchase Officer calls for total requirements from various government hospital pharmacies to generate schedule copy for e-tender
- Chairperson/Dean of Central Purchasing Authority invites medicine tenders after finalizing details of medicine e-tender with Superintendent of Pharmacy, subject experts, and also after accounts department has also thoroughly scrutinized it
- Tenders are advertised through newspapers and government portals
- Tender comprises two parts:
  a) Technical bid
  b) Commercial bid

- After tenders are invited, based on sample verification, detailed statements of technical observations are prepared by Superintendent of Pharmacy, along with recommendations from subject expert doctors

Analysis of commercial bid

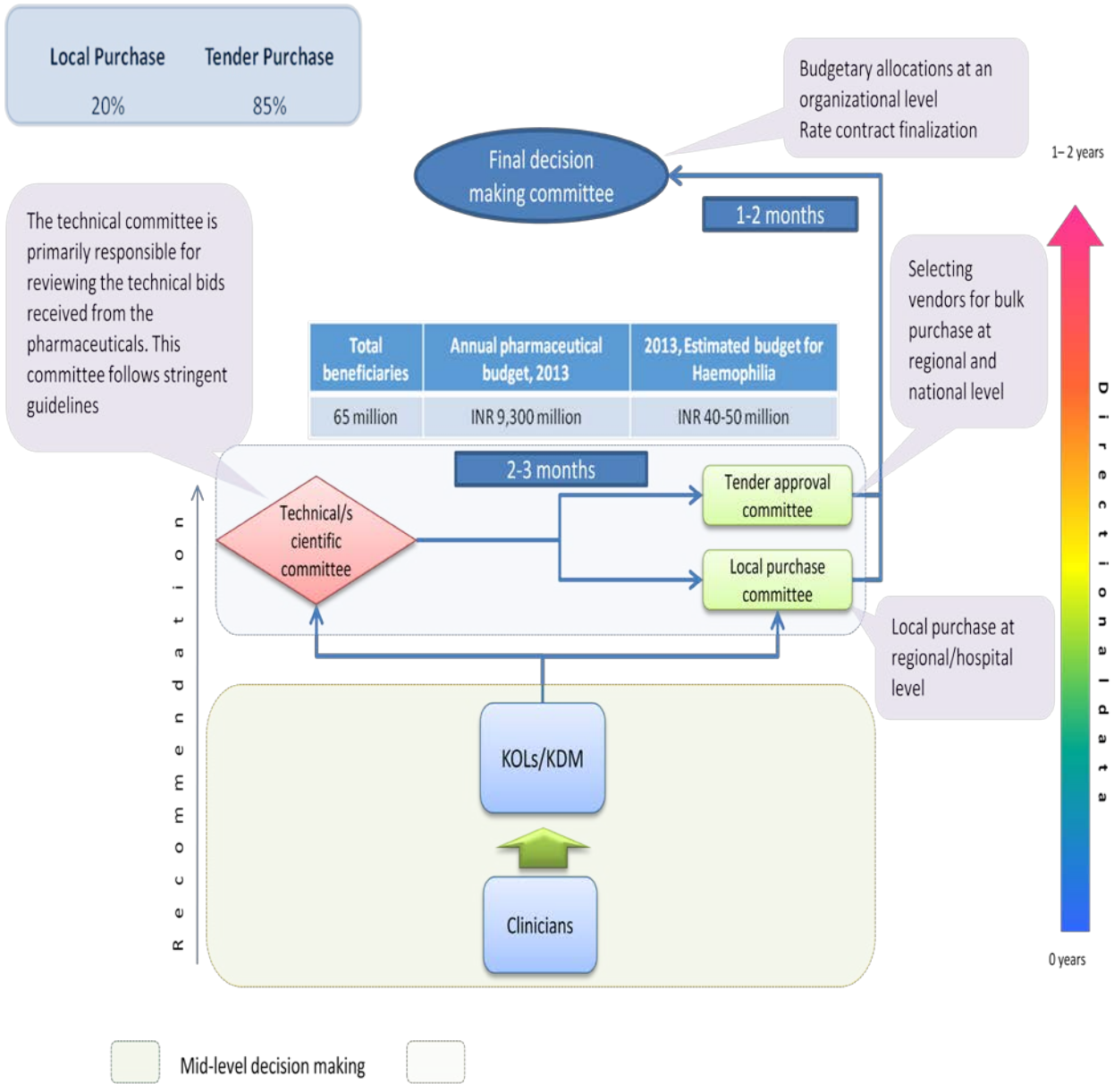
- Products that fulfill competent committee's technical requirements are qualified to be entered for bidding
- Closely assisted by Superintendent of Pharmacy and Chief Accountant, Chairperson finalizes tender winner on the basis of commercial bid
- Usually, supplier that has submitted the lowest bid is selected as long as all quality and efficacy parameters are at par

Execution of contract

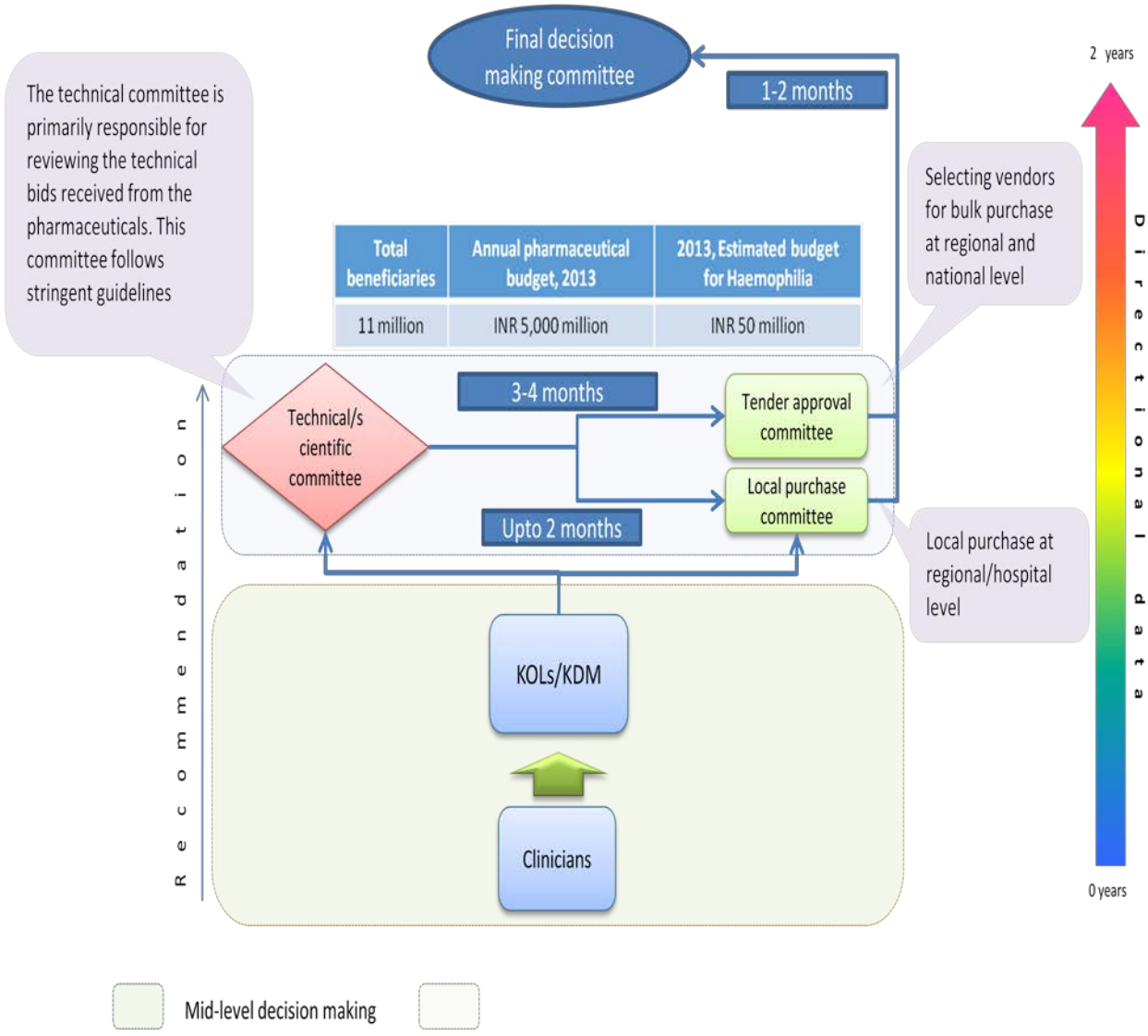
- After tender is assigned to the company, Assistant Purchase Manager executes and circulates rate circular to all hospital pharmacies

- Documents required to attach with tenders for imported products are embedded

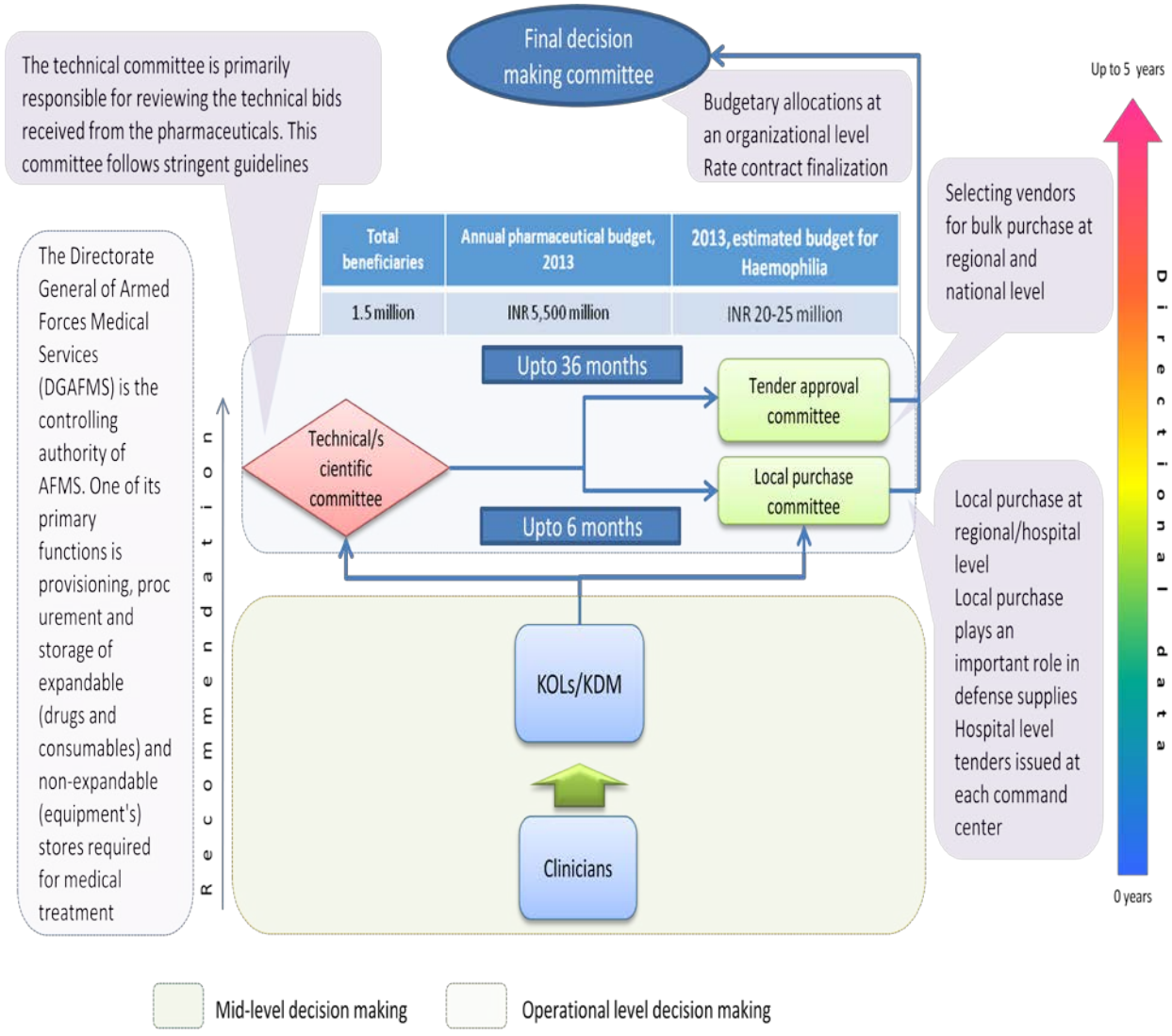
ESIC:


Local Purchase
20%
Tender Purchase
85%
Budgetary allocations at an organizational level
Rate contract finalization
Final decision making committee
1-2 months
1– 2 years
The technical committee is primarily responsible for reviewing the technical bids received from the pharmaceuticals. This committee follows stringent guidelines
Selecting vendors for bulk purchase at regional and national level
Total beneficiaries
Annual pharmaceutical budget, 2013
2013, Estimated budget for Haemophilia
65 million
INR 9,300 million
INR 40-50 million
2-3 months
Technical/s cientific committee
Tender approval committee
Local purchase committee
Local purchase at regional/hospital level
KOLs/KDM
Clinicians
Recommendation
Directional data
0 years
Mid-level decision making

RAILWAYS:


Final decision making committee
1-2 months
The technical committee is primarily responsible for reviewing the technical bids received from the pharmaceuticals. This committee follows stringent guidelines
Selecting vendors for bulk purchase at regional and national level
Total beneficiaries
Annual pharmaceutical budget, 2013
2013, Estimated budget for Haemophilia
11 million
INR 5,000 million
INR 50 million
3-4 months
Technical/s cientific committee
Tender approval committee
Local purchase committee
Upto 2 months
Local purchase at regional/hospital level
KOLs/KDM
Clinicians
Recommendation
2 years
Directional data
0 years
Mid-level decision making

DEFENSE:


Final decision making committee
The technical committee is primarily responsible for reviewing the technical bids received from the pharmaceuticals. This committee follows stringent guidelines
Budgetary allocations at an organizational level
Rate contract finalization
Selecting vendors for bulk purchase at regional and national level
Total beneficiaries
Annual pharmaceutical budget, 2013
2013, estimated budget for Haemophilia
1.5 million
INR 5,500 million
INR 20-25 million
Upto 36 months
Tender approval committee
Technical/scientific committee
Local purchase committee
Upto 6 months
The Directorate General of Armed Forces Medical Services (DGAFMS) is the controlling authority of AFMS. One of its primary functions is provisioning, procurement and storage of expandable (drugs and consumables) and non-expandable (equipment's) stores required for medical treatment
Recommendation
KOLs/KDM
Clinicians
Local purchase at regional/hospital level
Local purchase plays an important role in defense supplies
Hospital level tenders issued at each command center
Up to 5 years
Directional depth
0 years
Mid-level decision making
Operational level decision making

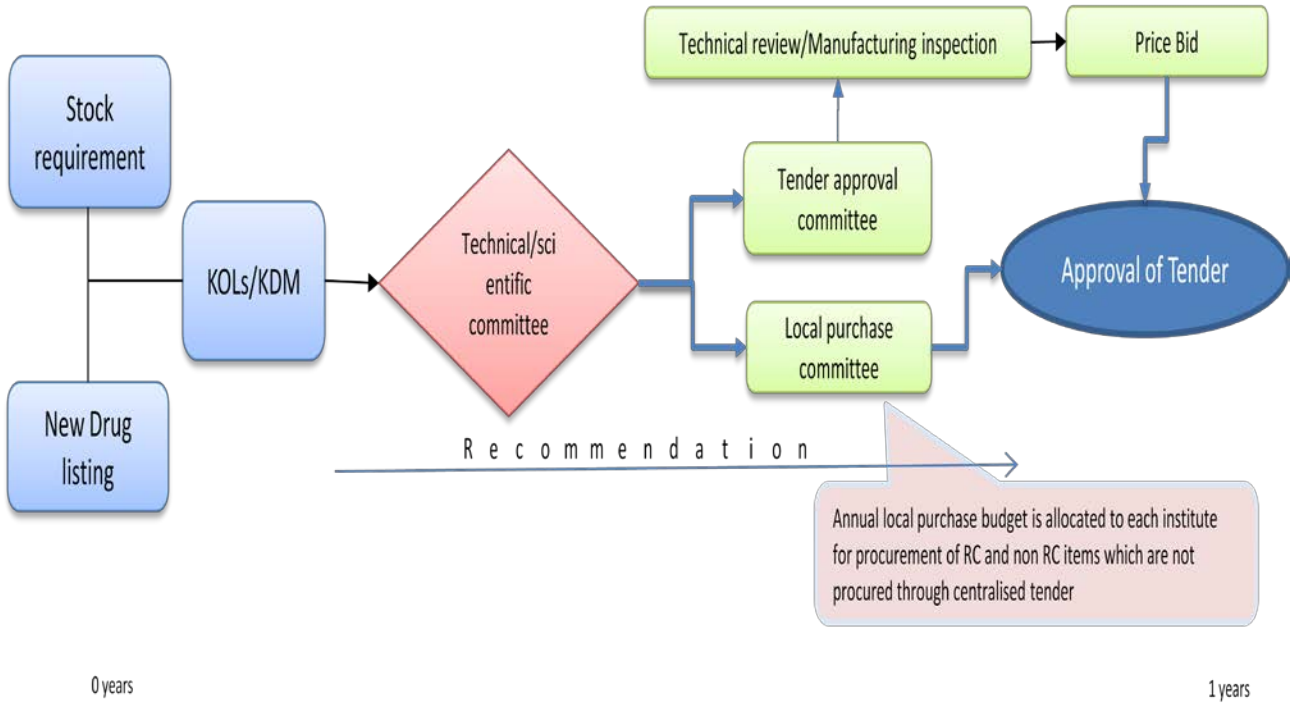
LISTING GUIDELINE OVERVIEW:

Key guidelines for tender listing and local purchase of drugs in Indian reimbursed organisation:

- For introduction of new molecule in the presence of already available molecules of the same cadre, listing of the brand requires minimum 3-5 years of standing in Indian market. Moreover this criteria is overruled in case of patented and exclusive drugs
- The firms will have to get registered with local and national drug control organisation
- Certificate of approval from Drug Controller General of India
- The firms must possess a valid Good Manufacturing Practices (GMP) certification and DGQA certificate for the quoted items or Valid import License
- Certificate for individual drug by state/central authority and have an annual turnover of more than INR 200-500 million for the last 3-5 years
- Every government reimbursement organisation maintains a list of commonly used medicines which are generally covered under the formulary and rate contract of the organisation. In case of non formulary items, each institute under the organisation is allocated with a certain budget for the procurement of the required drugs locally.

Organisation	Number of Hospitals	Haemophilia treatment centre
ESIC	34 Model Institutes, 117 Hospitals	34 Model Institutes
Railways	125 Hospitals	All headquarter units
Defence	11	All Centre
CGHS	254 Dispensaries, 47 empanelled hospitals	Hospitals under central government

STATE GOVERNMENT:



Tamilnadu Medical Services Corporation

- The Tamil Nadu Medical Services Corporation Limited is engaged in the procurement, storage and supply of drugs and medicines to the various Government Hospitals, Primary Health Centres and through them to the Health sub-centres throughout Tamil Nadu.
- Treatment and management of Haemophilia is available across all medical colleges in Tamil Nadu
- Drugs and factors for the treatment and management of Haemophilia are made available by TNMSC to all the listed centres through 25 warehouse and stores spread all across Tamil Nadu
- Procurement of AHF is done through tender process only
- TNMSC maintains 4 months physical stocks in its warehouses and 2 months stocks in pipeline for all the drugs
- TNMSC finalize the drug list every year by getting the requirements from the medical institutions these requirements are placed in the Drug Committee Meeting convened in the month of November every year
- The supply of selected drugs are allowed to be distributed to the hospitals as per the clearance of CDL, Kausuli. In addition to this, samples of the drug are drawn from the warehouses randomly and sent to the laboratories for analysis

Karnataka State Drug Logistics & Warehouse Society (KSDL&WS)

- Karnataka State Drug Logistics & Warehouse Society is responsible for the procurement of the drugs and medical supplies to the government institutes across 27 districts of the state
- Karnataka state government has 14 warehouses for drug and supplies storage
- KSDL&WS implement the logistical drugs and warehouse management to ensure the drugs of assured quantity are made available at all levels, up to the sub-center
- KSDL&WS also ensures to economize expenditure on drugs through pooled procurement system and helped to optimize accountability
- In the state capital, for treatment and management of Haemophilia, only KC General Hospital, maintains the stock of AHF which are provided for free to BPL patients and at subsidized rates for non BPL patients
- Victoria Hospital, Bangalore does not maintain any stock of the AHF from past 2-3 years
- Government medical institute face the issue of supply shortage in case of Haemophilia factors for instance KC General Hospital currently have factor XI (Hemonine) and Factor VIII inhibitor (Feiba); Factor VIII is out of stock and it generally takes around 2-3 months for the stock update in the hospitals
- Though the drugs for treatment and management of Hemophilia are included in the state government budget, the main factor for the non availability/shortage of the AHF in the hospitals of Bangalore could be attributed to low volume high cost treatment and lack of financial resources

Andhra Pradesh Drug Control Administration

- The Drugs Control Administration in the State offers services to the citizen as well as to manufactures and distributors of drugs
- Dr Batti Lala Meena is a Director General Drugs and Copyrights
- Management and treatment of Haemophilia is available in all the government teaching institute across state of Andhra Pradesh
- State government primarily procure the Haemophilia drugs (Factor VIII) from Baxter India trough tender process only
- Haemophilia Federation of India has 7 chapters in the state of Andhra Pradesh, out of which only 2 chapters i.e. Hyderabad and Vijayawada, are fully active and operational chapters.

Organisation	Identified patients	2013, Procurement value (in INR million)	2013, Procurement by local chapter of HFI (in INR million)
TNMSC	1,400	61	20
KSDL&WS	1,500	7.5	15-18
APDCA	2,900	13	18-20

- Government institutes generally face issues with supply shortage which is governed by internal logistic and financial scarcity

- TNMSC allocated INR 95 million in FY 2013 for the procurement of Haemophilia drugs and have only consumed INR 40 million till December 2013

- Many of the state governments like Government of Karnataka do not even allocate sufficient amount for the procurement of Haemophilia drugs considering the patient populations

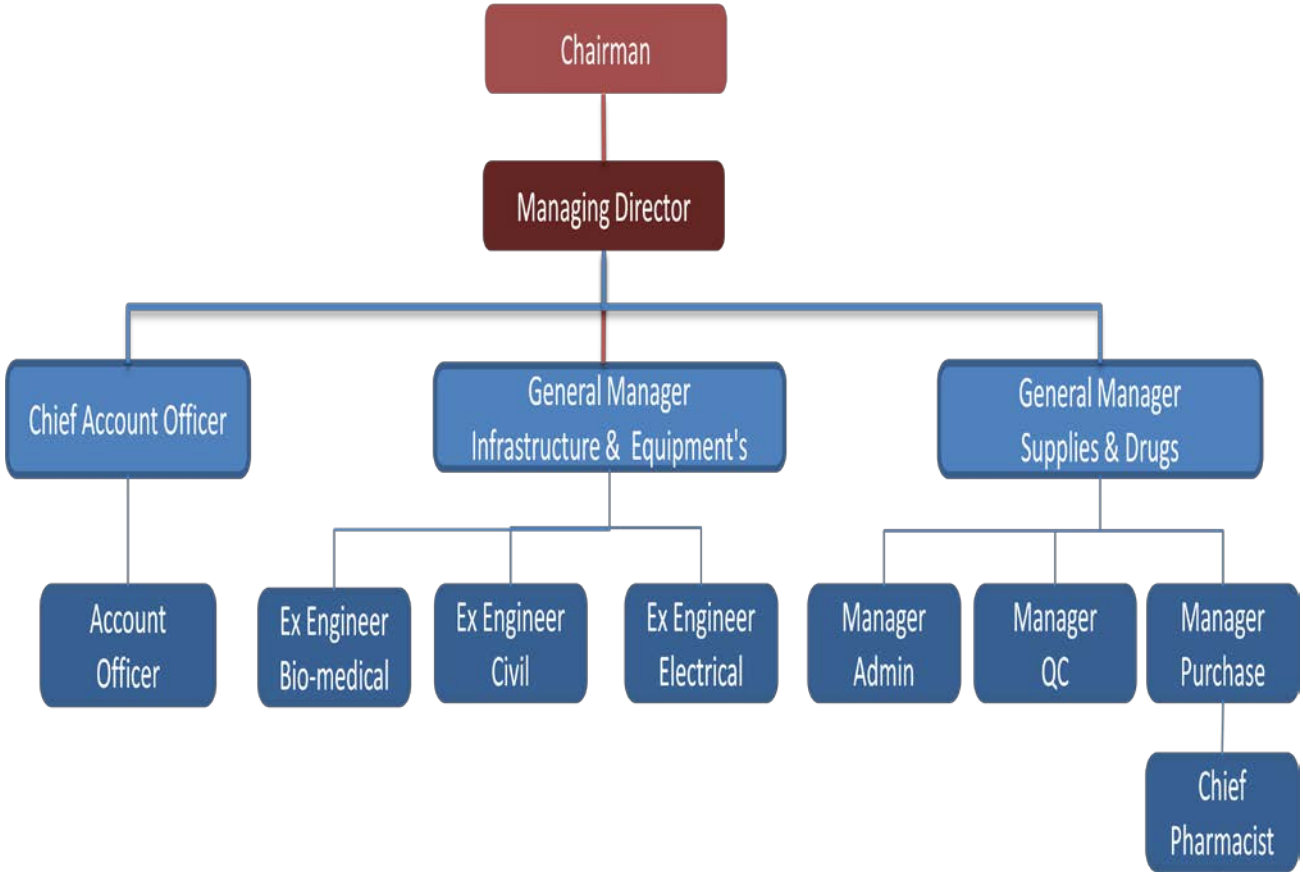
- In many cases patients are returned from the government medical institutes due to non availability of drugs or asked to procure the drug/factor from the open market

Overview of Drug procurement committee in State*

Board of Directors :

- Secretary, Health & Family Welfare (Chairman)
- Secretary, Finance Department
- Director Medical Education
- Director Medical Health Services
- Director of Drug Control
- Managing Director (Drug Corporation)

Organogram


Chairman
Managing Director
Chief Account Officer
General Manager Infrastructure & Equipment's
General Manager Supplies & Drugs
Account Officer
Ex Engineer Bio-medical
Ex Engineer Civil
Ex Engineer Electrical
Manager Admin
Manager QC
Manager Purchase
Chief Pharmacist

Unmet Needs and attitude assessment towards new products

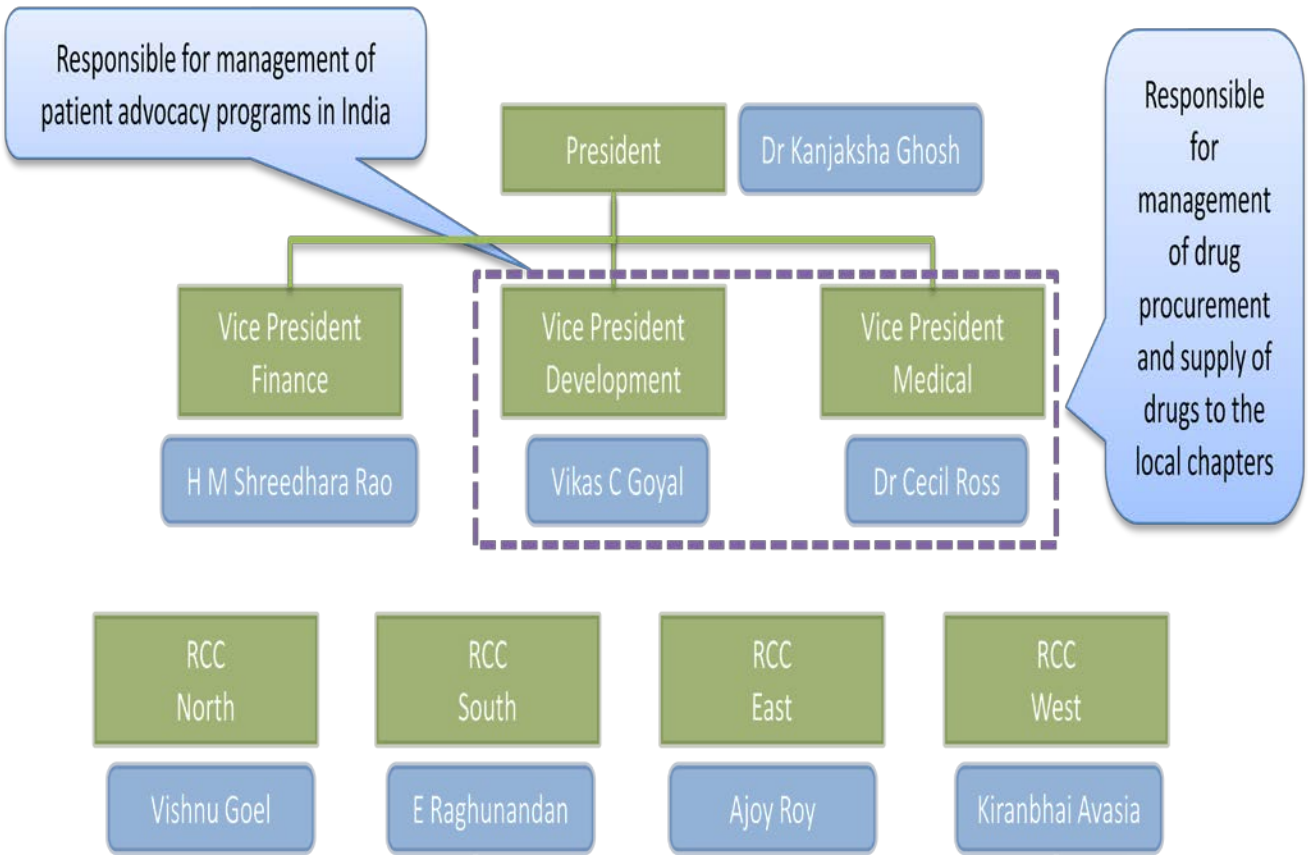
	Willingness to try	Not willing to try	Not sure
CGHS ↑↑↑	•If the product provides economical benefit •Clinical edge over the current treatment		↑↑ •Newer brands that are costly. May have clinical edge but
ESIC ↑↑	•If the product is available at lower costs thus can be used for longer duration of therapy	↑↑↑ •Costly brands	
Railway ↑↑	•If the product provides the benefit over the available brands		
AFMSD ↑↑	•If the product provides the benefit over the available brands and have proven clinical advantage over the available treatment		
State Government ↑	•It will be based on the cost economic outcome of the product	↑↑ •If the product is costlier than the current available product	

Degree of response

↑ **Low** ↑↑ **Moderate** ↑↑↑ **High**

Hemophilia Support Organizations

- HFI was established in 1983 it is a self-help NGO run by Persons with Haemophilia themselves. HFI represent India as National Member Organization at the World Federation of Haemophilia based in Canada. It also work in close collaboration with World Health Organization (WHO) and National Aids Control Organization
- HFI operates in India through 72 chapters (48 affiliated and 24 non-affiliated chapters) across the country
- In year 2013, HFI focused on activation of inactive or partially active chapter across India. For this an executive team was formulated which visited the chapters to understand and resolve their practical issues and challenges
- HFI in collaboration with AIIMS, NIIH-Mumbai and St. Johns Medical College has initiated the inhibitor screening program to have a periodic checking of inhibitor at least after 50 exposure days
- Procure AHF products majorly from **Baxter India and Novo Nordisk** and provide to patients on economical rates or for free to economically challenges patients



Procurement Agreement

- HFI currently is only procuring products from Baxter India
- Haemophilia Federation of India gets into MoU (undertaking) with the pharmaceutical company. This agreement entails details of minimum quantity that HFI commits to procure within the stipulated duration of the agreement
- On the basis of the commitment Baxter India in turn provides 30% of the unit for free of cost

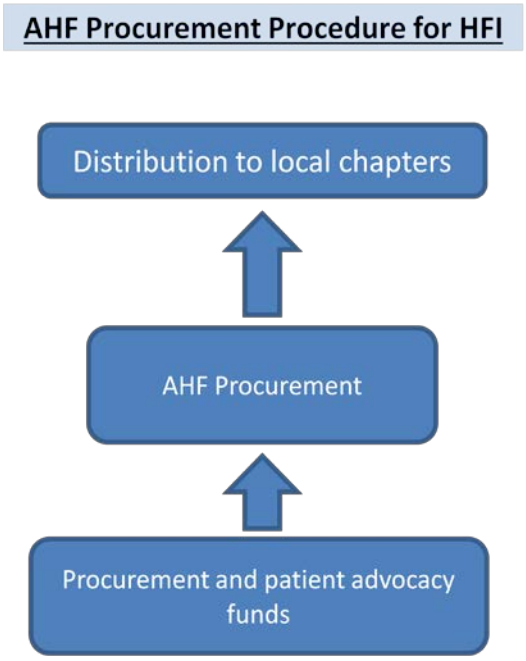
Distribution

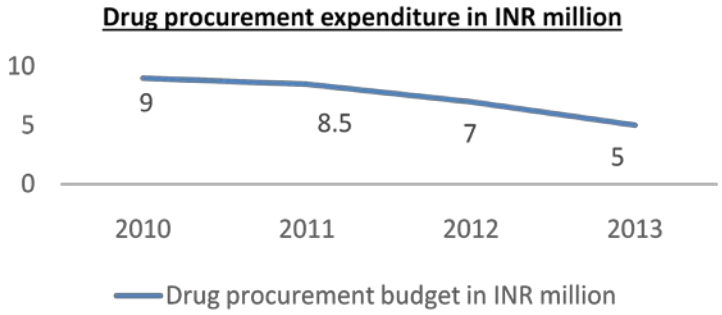
- Indentation for all chapters across India is carried out at Delhi office, however delivery is made by local distributors to various chapters on need basis
- Since all chapters are locally based out of hospitals, the factors are stored in the cold storage facilities of those respective hospitals

Fund Raising

HFI is currently managing the funds through donations, fund raising activities and support from international organisations.

HFI Procurement Procedure for anti hemophilia factors





HFI AHF Procurement trend:

- Procurement of factor VIII and IX by HFI is consistently been declining for the last 3-4 years
- Maximum procurement achieved was around INR 9 million in 2010
- Reasons for decline are:
  - Paucity of funds
  - Availability of factors in government institutes
  - Non supportive behaviour of Pharmaceutical companies
- HFI provide total quality care, education and treatment at affordable cost, psychosocial support and economic rehabilitation to the patient. On 17 April,2013 HFI organised a walk from Janpath to Boat Club, Delhi and distributed haemophilia awareness and education material
- Provide training through CME, Workshops and training seminar for the clinicians and paramedical professionals to keep them updated and maintain competency level
- Two international Haemophilia Training Centres at CMC Vellore and KEM Hospital Mumbai
- HFI maintains national haemophilia registry which is fully functional and approved by the Institutional Ethical Review Board of St. John's Medical College & Hospital, Bangalore

- **Associations:**
  - Baxter India
  - Novo Nordisk
  - HANS Foundation
  - ONGC (Oil and Natural Gas Corporation)
  - SAIL (Steel Authority of India)
  - CANON
  - Give India
  - Nestle India

- **Patient Advocacy Programs:**
  - Medical assistance to children and person with Haemophilia
  - Carrier detection test for unmarried women and pre-natal diagnosis for female haemophiliacs
  - Financial support to haemophiliac families
  - Provide Anti-Haemophilic factors to patients for free or subsidized rates
  - Education and awareness campaigns
  - Educations support to Haemophilia children's
  - Providing alternative treatment support to patients

- **HFI does not receive any kind of financial aid from government of India rather certain government undertakings like ONCG, BHEL and so on provide assistance to HFI in organizing camps and advocacy program for Hemophilia**

- HFI is consistently making efforts for the rights of patients and has filed PIL in state high courts for approval and establishment of Hemophilia centers across every state in the country

HFI Anti Haemophilia Factors procurement and supply rates

Factor	Procurement rate (Per unit in INR)	Price to Patient (Per unit in INR)*
VIII	10	0 to 12
IX	18	0 to 20

** Price to patient depends on the payer capacity*

Availability of Haemophilia treatment post intervention of HFI

Complete treatment	Partial treatment	PIL/Lobbying in progress	PIL to be filed
- Jammu &Kashmir	- Jharkhand	- Punjab	- Chhattisgarh
- Uttar Pradesh	- Maharashtra	- West Bengal	- Nagaland
- Uttarakhand	- Karnataka	- Orissa	- Mizoram
- Tamil Nadu	- Andhra Pradesh		- Tripura
- Gujarat	- Kerala		- Arunachal Pradesh
- Goa			- Meghalaya
- Rajasthan			- Manipur
- Haryana			
- Delhi			
- Bihar			
- Assam			

As the state government and central government is taking initiatives for establishment of treatment and management centres for Haemophilia, the over all market for AHF is likely to see an expansion due to increase in budgetary allocations for the procurement of drugs, in near future

Hemophilia patient's welfare society:

- It is a non-profit organisation based out of Lucknow which works for the welfare of people suffering with a genetic disorder haemophilia
- Provide education and information about Haemophilia care, to make treatment available at affordable cost
- Provide AHF at subsidised cost
- Provide support by locating undiagnosed person, provide carrier detection test and prenatal diagnosis
- After intervention of UP High Court, society has brought about INR 135 lakhs in year 2011 from state government

Government support

- The central government will provide financial assistance under the National Rural Health Mission (NRHM) to state governments to help haemophilia patients
- State governments were invited by the centre to submit proposals for treatment of haemophilia cases in their respective programme implementation plans for consideration of assistance
- Indian Railways provide discounts to Haemophilia patients on travelling.

Barriers and Enablers

Barriers:

- High cost of therapy
- Poor patient compliance and adherence to the treatment
- Limited options for the patients with inhibitors, available options pose major economic challenge
- Lack of awareness and knowledge
- Non-availability of the AHF in remote areas
- Lack of early treatment and prophylaxis options
- Storage and administration of clotting agents
- Approach to Hemophilia Treatment Centre is difficult for the patients from remote areas and for those with lack of transportation, and with crippling physical disabilities

Enablers:

- Better diagnosis and improved treatment options
- Improved standard of care
- Increased numbers of Hemophilia Treatment Centers
- Improved safety of AHF; Recombinant AHF
- Development of Inhibitors
- Initiative by state and central government for development of infrastructure for the treatment

NHR UPDATE

National Hemophilia Registry, a database of all the PWH in India is fully functional on beta (per-release) stage. Our registry is approved by Institutional Ethical Review Board of St. John's Medical College & Hospital. IERB Study

Reference number 54/2012.

Registry team is as follows:

Medical/Clinical Team:

(Prof.) Dr. Kanjaksha Ghosh, President, HFI and Director of Institute of Immunohematology, KEM Hospital, Mumbai

Dr. Cecil Ross, Professor of Medicine Hematology, St. John's Medical College & Hospital, Bangalore

Co-ordination and Review Team

Mr. Vikash Goel (VPD) HFI

Requirement & User Experience Architect

Mr. Premroop Alva (PWH), Director Tranquil Residences

Technical Architect

Mr. SomuShekar (PWH), Director Tatwaa & IT consultantCentralized web application which is developed as per the guidelines of HFI-Medical Advisory Board and IT standards can be accessed via Internet. Hosted domain is http://www.hemophiliaregistry.in. Application is built on secured industry standard opensource stack which is widely accepted by Google, Yahoo, Facebook.

All our 78 chapters in India are trained for management of web-application, reporting and day-to-day activities of registry. Looking into longterm effective management of registry, we have involved our Women's and Youth's group in our trainings. Involvement of our women and youth has provided opportunities to our hemophilia family; at the same time this will add value to a great extent in next phases like factor management, rehabilitation management, special hemophilia care.

Conclusion

- There are more than one lakh patients of hemophilia in india but only 10-15% of paitents are diagnosed and registered.

- Management and treatment of patient becomes very critical as clinicians are not able to diagnose the problem first hand and the treatment delays significantly.

- Females are usually only carriers of Hemophilia and are unlikely to be affected by the condition.

- Bleeding disorder percentage gender wise can be represented as 97% for women and only 3% for men.

- Zone wise prevalence of hemophilia are found to be depicted as 38% south , 24% north , 23% west and 15% east.

- Due to the high cost of AHF, most patients in India may be required to take infusions of unsafe, wet blood products such as **Fresh Frozen Plasma (FFP)** or lyophilized cryoprecipitate. This necessity exposes patients to blood borne infections like HIV/AIDS and Hepatitis .

- Of the total patient receiving factor concentrates almost 98% cases seek treatment on need basis, and a maximum of 1 % to 2% patients take prophylactic therapy, which is also determined by the socio economic status of the patients.

- The overall market for clotting factors comprising of anti-haemophilic factors, blood plasma products and cryoprecipitate was estimated to be INR 1,480 million in year 2013.

- The market share for clotting factors was estimated to be around 52% in 2013 and is expected to grow with a rate of 7% by 2015 reaching up to INR 943 million.

- Clotting factors are primarily used for management of Hemophilia, moreover they also have utility in other conditions such as Surgeries, trauma, burns, oncology and so on.
- In India, major companies which are active in Anti Hemophilia Factor segment are Baxter and Novo Nordisk.

- Reliance is also present in the segment with a Factor VIII product "Hemorel". Hemorel is an imported product and have supply and shortage issues due to on and off import of the product .

- The cost of AHF varies from the type of injury and episode to episode. For instance, a simple injury may be treated by 2,000-2,500 units of AHF for a 50 kg body weight, but severe injury like intracranial injury can call for 30,000 units of AHF which will cost around INR 2 lakh.

- As Haemophilia is a low volume high value disease, irrespective of income slab, majority of the patients seek assistance from government/reimbursement organisations or HFI.

- AHF being very costly product, various NGO's and Hospitals are actively providing the therapy either free-of-cost or at affordable/subsidised prices to the patients . Hemophilia Society is one such example which procures AHF directly from the company at discounted prices and provides the same to the customer at economical rates or for free (depending on the patient affordability).

- In case the patient purchase the AHF directly from dstributors, retailer/Hospital margins are passed on to patient as discounts. Baxter India provides a discount of 22%-25% on MRP to patients and NGOs .

- Under government Hemophilia aid program, patients under BPL are provided with free medicines for the management of the disorder, whereas patients within income group of INR 2-5 lakh have to bear 30-50% of the product cost.

- Due to the time constraint of the study we are unable to deliver few objective of the project which had been already informed to our client.

ANNEXURE

Strategic Plan for coming two years:

India has 650 districts (with a 2 million population). Each district has 200-250 beds in district hospitals represented by broad clinical specialists and a blood bank. In addition, there are 150 medical colleges run by the State governments in this country.

The medical colleges tend to have better management facilities and many super specialties. Unfortunately haematology as a super specialty is new in this country and not more than 30 medical colleges can boast of this super specialty.

Blood banking service is present in all the medical colleges. In addition, India is producing 20-25 fresh haematology super specialists each year. At least one third of them may eventually man the govt. hospitals in this country. While there is a lot to be desired in these medical colleges and govt. hospitals, when each state govt. offers their help for PWH, it is through these machinery that health care system of PWH will be delivered. Thus HFI will have to engage these institutions, State Govt., Federal Govt. Institutions and high quality autonomous medical institutions (govt. run) like AIIMS, PGIMER, BHU etc. to help the hemophiliacs. It has plan to have 10 such autonomous institutes spread over the country is in the next 5 year plan. Over last 25 years, HFI has already developed or associated itself with the development of Hemophilia Care facilities for 74 of its chapters across the country.

HFI along with its chapters in coming years will try to build on and develop existing facilities and ensure that those will not be allowed to be withered away rather will be developed further.

At each of this centers i.e. district hospitals, medical colleges and apex centres, hemophilia Care will be coordinated by HFI or its chapters for their smooth functioning. These chapters and HFI will mainly function as the facilitating interface between PWH and the Govt organization. In addition these chapters will also over see all the interactions with local authorities i.e. Municipality, Corporation etc.

Programmes:

Coming to the Programme for the coming two years, HFI does not have the financial, logistic or man power capabilities of developing all the 650 district level treatment centers or 150 govt. medical colleges which are distributed across the country. However, HFI will approach the challenge in coming two years, in the following ways:

1.Engaging or advising govt. to provide:

a.'Otherwiseable' certification for PWH with severe disease (already initiated)

b. More NHTC's can be formed for developing and training manpower for management of PWH across the country

c. Specify the amount allocated for hemophilia on National Rural /Urban Health Mission Scheme for state govt.

d. Involve Autonomous Central govt. Health Care Institutions for haemophilia care through involvement of local chapters in that area.

2. Improving Human Resources for haemophilia Care:

This will be done by HFI at several levels.

a. Twinning a treatment center will be done with NHTCs

b. Fellowships. Individuals involved with haemophilia care who wants to increase his/her skills in particular

area of training.

c. Strengthening and increasing the number of National Hemophilia Training Centers (NHTCs). (Presently Medical College-Kolkata, St John's Bangalore, AIIMS Delhi). This will be increased to 8 in coming two years i. e. PGIMER-Chandigarh, BHU-Varanasi, Calicut Medical College-Kerala, Guwahati Medical College-Assam & SCB Medical College (Cuttack), NIMS.

d. CME in each area, targeting doctors from various facets of life (to increase awareness among doctors). This will be done in collaboration with state blood Transfusion Council.

e. Workshop. This will involve hand on training for (i) Physiotherapists (ii) Laboratory Technicians (iii) Orthopedic Surgeons etc. This will be done by HFI industry liaison (funded by industries).

f. HFI-Medical Societies of India linkage. There are several medical societies who hold regular annual conferences. They will be engaging to involve a topic or two in the field of coagulation disorders and hemophilia during their annual scientific conferences. (These medical organizations of interest are Indian Medical Association, Indian Academy of Pediatrics, Federation of Obstetrics and Gynaecological Societies of India, Dental Surgeons, Public Health Association and Associations of Orthopedics Surgeons and physical therapists.)

At present this linkage is weak and individual chapters have to occasionally involve one or two such societies in this programme. In coming two years this programme will be a regular affair.

g. Developing at least one Apex Center at each state (30 i.e. one in each state.). The main bureaucrat involved in administering health care is Health Secretary. HFI with its chapters will engage health secretary's office in each state so that each state can develop at least one good center (Apex Center for State) for overall haemophilia care. Small states or union territories like Delhi, Chandigarh, Goa, Tripura are such that one apex center may function both as training center and state level health treatment center.

h. Finishing the unfinished agenda of engaging state govt through human rights litigations/PIL.

Through advocacy and/or using this route already being followed, State Govt. has been made partially or fully responsible for hemophilia care. These states are New Delhi, Karnataka, Tamil Nadu, Pondicherry, Kerala, Gujarat, Bihar, Assam, Rajasthan, Goa (13/31 states). There are 9 states in north eastern part of the country; except Assam other 7 states are yet to give relief to PWH. These states' development lags behind because of insurgencies and other facts. HFI will have very little impact in these states in coming 2 years. However, efforts will be continued.

i. Hemophilia Registry is developing well and it will go a long way in relieving some of the states of this country who have not yet committed themselves to care of PWH of HFI.

j. Finding out undiagnosed PWH in the country and bringing them to the fold of HFI for better care.

Novonordisk has already supported a project in Manipal to this effect. Indian Council of Medical Research is also involving a sub-divisional town in Maharashtra where house to house verbal autopsy is undertaken to find out presence of severe haemophilia in the

house hold by routine lay health care workers. Once verbal autopsy is done, the pilot project will give us an idea of extending this project slowly to rest of our rural areas (70-80% of India).

k. Engaging Indian Council of Medical Research in Technical/Man Power development. National Institute of Immunohaematology (NIIH) and ICMR institute are already working intensively on bleeding disorders in this country and regularly training manpower and helps laboratories in need of help for coagulation disorders. Specially ICMR has provided 3 million rupees as project for treating and developing hemophilia lab in some backward states. This effort will continue in coming 2 years.

m. There are several govt. funding agencies in this country who provides funds for research. SCIR, DST, ICMR are some such institutes. HFI as they try to develop along with apex centers. Developing Haemophilia Care Comprehensively across Indian subcontinent is a gargantuan task considering the obstacles at every level of govt. health care system and public administration. There is also lack of general development of medical care in the length and breadth of this country; under such circumstances it is not expected that only haemophilia care will be an island of excellence in the Govt hospitals while general health care remains wanting in many areas. However we will not leave any stone unturned to improve haemophilia care across the country using all of the above tools as described above.

Hemophilia Comprehensive Care included in the 12th Five Year Plan:

- Govt. of India has included hemophilia care in 12th five year plan which will provide comprehensive care services including diagnosis and management of hemophilia in 120 medical colleges throughout the country
- Central government under the NRHM has approved INR 32.4 million for treatment of Hemophilia in the state of Haryana
- State government has designated general hospitals of Gurgaon, Karnal, Ambala, Hisar, and Rohtak where the treatment of Hemophilia would be available
- Central government under NRHM allocated INR 11 million and INR 32.4 million for Hemophilia treatment to government of Jharkhand and government of Maharashtra, respectively
- Rashtriya Bal Swasthaya Karyakram (RBSK) under NRHM provides facility for early detection and treatment of Haemophilia
- It is considered as a great achievement of HFI which had been lobbying with the Govt. for last two years
- From 23rd to 24th February 2013, HFI organized a National Hemophilia Care Meet at Hotel Ashoka, Bangalore. The meet was sponsored by **Novo Nordisk** and was jointly organized by HFI, CMC & Saint John's. Approx. 120 participants including medical experts.

Hemophilia Annual General Body Meeting:

- Annual General Body Meeting 2013 was held on September 28th & 30th 2013 ad Vishwa Yuvak Kendra, New Delhi. More then 150 patients, their families and doctors were present on this 2 day event which consist of trainings, presentations and awards were given to patient

Salient features of HFI report filed for Public Interest Litigation

- For the Dept. Health, Govt. of NCT of Delhi:
- An AHF facility to be set up in 3 hospitals, namely Lok Nayak, DDU and GTB hospital.
- All BPL (below poverty line) families will be provided free AHF
- In emergency cases of emergency, free treatment to all Haemophilia patients in the designated hospitals.
- Graded payment system in respect of APL (above poverty line) patients with minimum 3 years domicile in Delhi:
- Family income up to Rs. 200,000 per annum – 20% cost of AHF
    - Family income up to Rs. 250,000 per annum – 50% of cost of AHF
    - Family income above Rs. 500,000 per annum - full cost of AHF to be borne by the patient
- Central Government hospitals functioning in Delhi to provide AHF free to BPL category and to patients in emergency.
- Monthly clinics to be started shortly in Safdarjang and Kalawati hospital

Split of Patients on the basis of On Demand (OD) vs Prophylactic therapy vs Severity of Haemophilia (n=10)

Severity	Therapy	% of patients
Mild	OD	30%
Moderate	OD	20%
Severe	OD	50%

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