



Irish Haemophilia Society

Introduction to Haemophilia

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- Introduction to Haemophilia
- Introduction to Von Willebrand's Disease
- Inheritance
- Bleeding patterns
- Introduction to Factor replacement therapy
 - Plasma derived and Recombinant products
 - Prophylaxis v On Demand
- Organisation of care
- HIV and Hepatitis C
- Current and future threats
- Risk Communication
- Future developments



Bleeding

- Aura
- Pain, Heat, Swelling
- Damage
- Early treatment





Haemophilia A

- FVIII deficiency
- 105 per million males
- 1.05 per 10,000 males
- 80% of Haemophilia





Haemophilia B

- FIX Deficiency
- 28 pre million males
- 0.28 per 10,000 males
- 20% of Haemophilia



Figure 8. Tsarevich Alexis.



Haemophilia -Severity

- Severe < 1%
- Moderate 1 to 5 %
- Mild 5 to 40%
- Severe - spontaneous bleeds





Von Willebrands

- Type 1 - Mild
- Type 2A - Moderate
- Type 2B
- Type 2N
- Type 3 - Severe

0.1% of Population





Ireland

- Haemophilia A 410
- Haemophilia B 203
- VWD 918
- Other 510



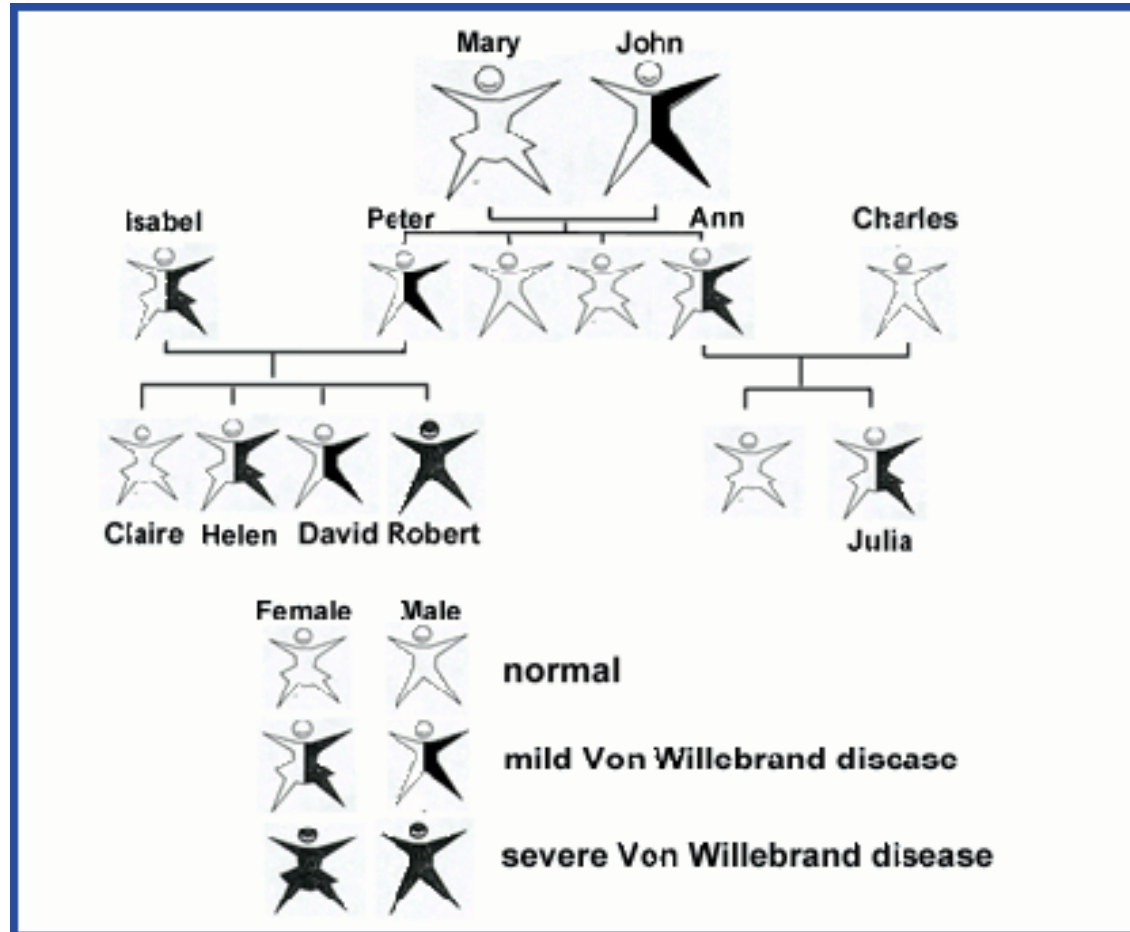


Inheritance of Haemophilia

- **Sex linked Inheritance**
 - X chromosome
- **Carrier mother**
 - Sons 50% chance, haemophilia
 - Daughters 50% chance, carriers
- **Man with Haemophilia**
 - Sons, no haemophilia
 - Daughters, obligatory carriers
- **30% Spontaneous Mutation**



VWD Inheritance

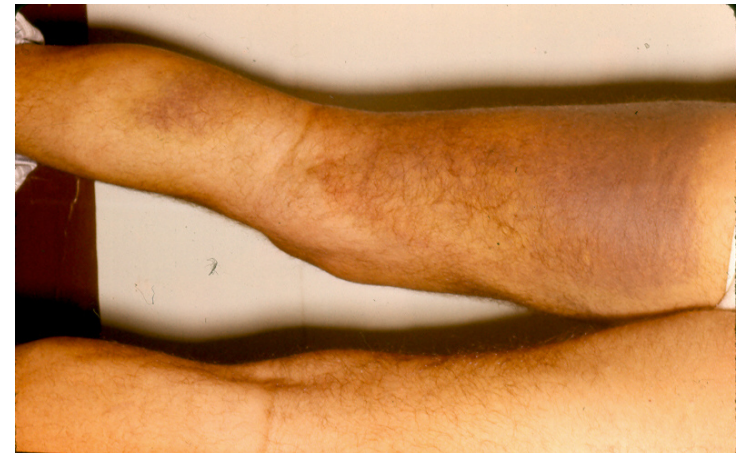




Bleeding

Serious

- Joints (haemarthrosis)
- Muscle/soft tissue
- Mouth/gums/nose
- Haematuria





Bleeding

Life Threatening

Central Nervous System

Gastrointestinal

Neck/Throat

Severe Trauma



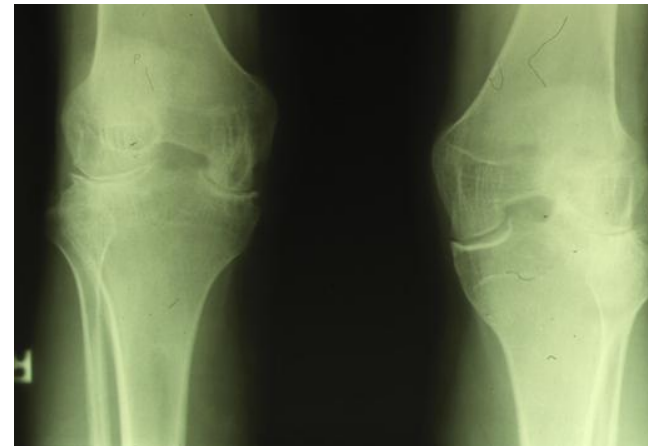
Incidence of bleeding into joints

- Knee 45%
- Elbow 30%
- Ankle 15%
- Shoulder 3%
- Wrist 3%
- Hip 2%
- Other 2%

- Target Joints



The musculoskeletal consequences of “undertreatment”





“Target” joint, Chronic Synovitis





Advanced state of haemophilic arthropathy





Treatment Principles

- Prevention of bleeding should be the goal - Prophylaxis
- Treat acute bleeds early
- Home therapy – early treatment
- Severe bleeds – hospital
- Avoid aspirin, Intramuscular injections, non steroidal anti-inflammatory agents
- Treat with Factor Concentrates



Development of Replacement Therapy

- | | |
|--------|--|
| 1960's | <ul style="list-style-type: none">- Plasma- Cryoprecipitate |
| 1970's | <ul style="list-style-type: none">- Cryoprecipitate- Factor Concentrates- Prothrombin Complex Concentrates |
| 1980's | <ul style="list-style-type: none">- Concentrates- Virally inactivated concentrates |





Development of Replacement Therapy

1990's

- High Purity Concentrates
- Recombinant concentrates
- DDAVP

2000's

- 2nd Generation Recombinant
- 3rd Generation recombinant



Plasma-derived Concentrate

- Manufactured from plasma
- Virally inactivated
- Excellent safety record since 1991
- Donor selection
- Donor screening (tests)
- Good manufacturing practice
- Viral inactivation
- Post use surveillance



Recombinant Concentrates

- Manufactured from cell bank with recombined gene
 - Viral inactivation
 - No viral transmissions since use in 1994
-
- 1st Generation
 - 2nd Generation
 - 3rd Generation



On Demand Therapy

- Treat bleeding episodes
- Treat early
- Home treatment
 - Clinical management



Prophylaxis

- **Prevention**

Maintain level $> 1\%$

FVIII - 3 times weekly

FIX - 2 times weekly

CVAD devices

Secondary prophylaxis

- Target joint
- Life event





Factor replacement therapy

Outcome at different doses

| | France (‘on demand’) | The Netherlands (intermediate- dose prophylaxis) | Sweden (high-dose prophylaxis) |
|--|-------------------------|--|--------------------------------------|
| Numbers | 116 | 21 | 19 |
| Age at study analysis | 23 | 21 | 16–22 |
| Age at start of home treatment | 8.9 | 9.1 | NA |
| Age at start of prophylaxis | NA | 4.6 | 2.6 |
| Annual number of joint bleeds | 16.3 | 5.3 | 3 |
| Pettersson score | 18.8 | 6.0 | 6.5 |
| Orthopaedic joint score | 7.7 | 2.0 | 2.4 |
| Clotting consumption (IU/kg/year) | 1634 | 1828 | 3713 |



Manco Johnson Study - Prophylaxis New England Journal of Medicine 2007

- Data on 65 children with Haemophilia collected over 5 years
- On –demand v Prophylaxis
- 93% on Prophylaxis had normal joints
- 55% On- Demand had normal joints
- **Prophylaxis associated with 83% reduction in joint damage**



Manco Johnson Study

- Prophylaxis New England Journal of Medicine 2007

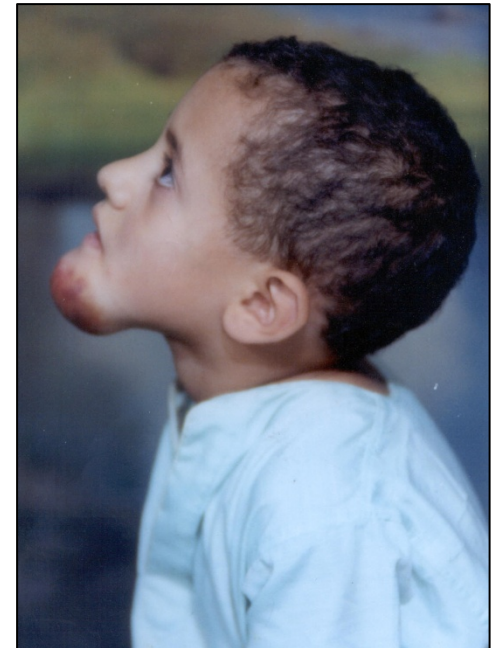
- 18 abnormal joints in 15 Children
- 13/15 were on demand
- 2/15 were on Prophylaxis

Study demonstrates conclusively that Prophylaxis is effective at preventing joint bleeds and preserving joint function and structure in young boys with Haemophilia A.



Minimum “Survival” standard

- Treatment in a care centre
- Safe and efficacious replacement therapy
- Factor concentrates for:
 - Life / Limb threatening bleeding episodes
 - Surgery
 - Major bleeding episodes





Good Standard of Care

- Treatment in a comprehensive care centre
- Provision of safe and efficacious replacement therapy
- Home treatment
- 'On Demand' therapy



Optimum Haemophilia Care

- Treatment in a comprehensive care centre
- Provision of safe and efficacious replacement therapy
- Home treatment
- Prophylaxis
- Educated and involved patients / Parents



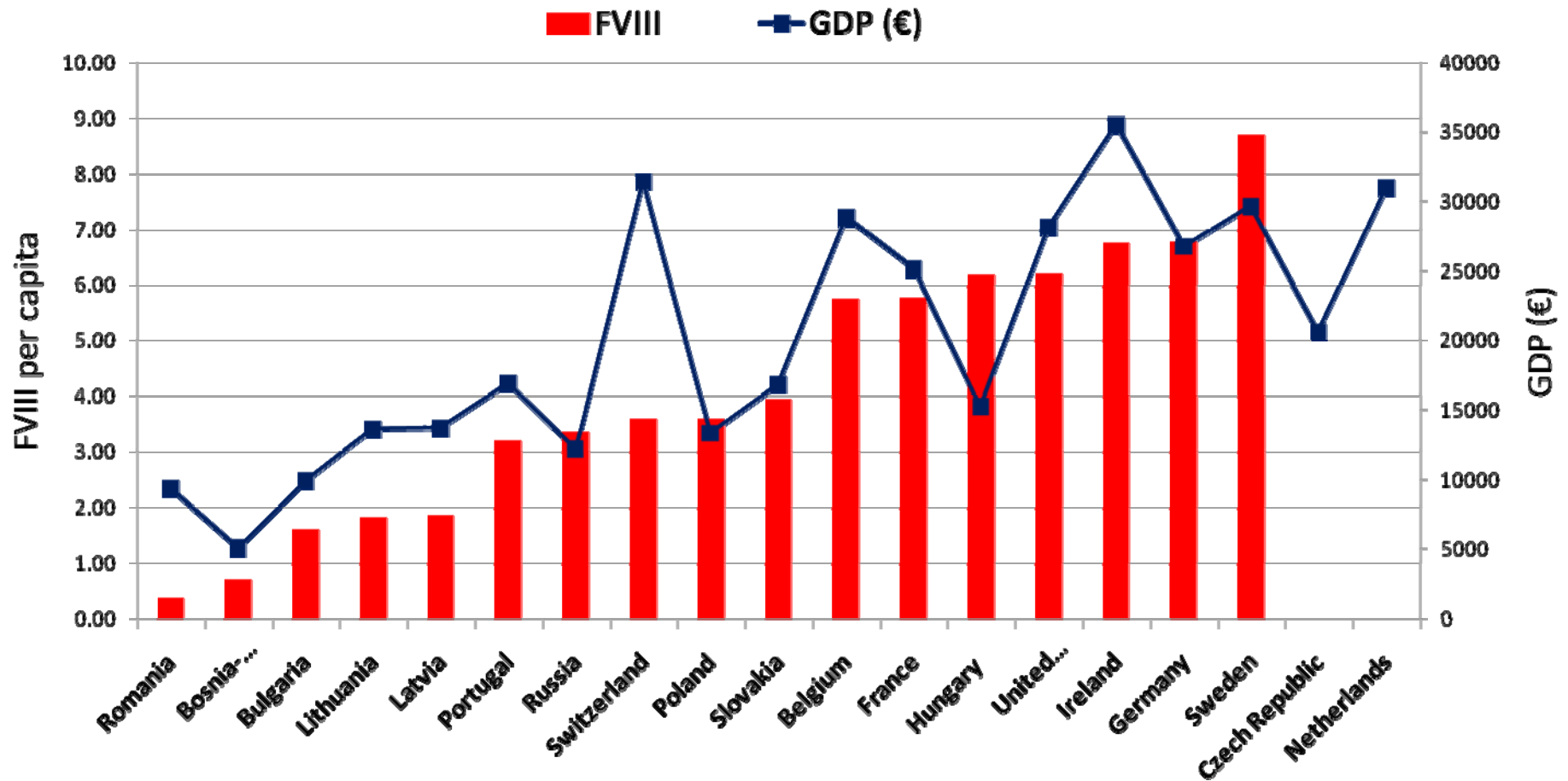
Objectives of Treatment-

As Access to replacement Therapy increases:

| <u>Objective</u> | <u>Per Capita FVIII use</u> |
|-------------------------------|-----------------------------|
| Survival | 0 – 1 |
| Functional Independence | 1 – 3 |
| Joint Integrity | 3 – 6 |
| Full integration into Society | 5 – 7 |



Concentrate Use per capita





Different Reality and perception – Optimum Care

Child :

- Normal life expectancy
- Avoid joint damage
- Normal education, career prospects
- Prophylaxis





Different Reality and perception – Optimum Care

Young Adult :

- No further joint damage
- Education, career prospects better
- Hepatitis C
 - Better treatment in 10 years
 - Relationships, lifestyle
 - Engage with peers, community





Different Reality and perception – Optimum Care

Older Adults (+ 45 yrs)

- Joint surgery, replacement
- Careers defined by past
- Better HIV therapy, survival
- More aggressive HCV therapy
- First generation who have to consider disease of old age: heart disease, cancer
- First generation to have grandchildren with haemophilia








I.H.S. Educational DVD


DVD COVER 11th Sept 07.step new 11/09/2007 09:46 Page 1


PERSONAL STORIES OF LIVING WITH HAEMOPHILIA

 Gerard O'Reilly was born in 1959 and raised in rural Ireland in a town called Freshford, Co. Kilkenny. Gerard tells his story of living with haemophilia in the 1960's and 1970's.

 Michael Loughane lives in rural Ireland. He gives an account of the differing experiences of his son Vincent and grandson Paul who were both born with haemophilia in different decades.

 Kevin Birkett is father to 8 year old Conor who has haemophilia B. Kevin tells his story about living with haemophilia.

 Declan Noone is 25 years of age and has severe haemophilia A. Declan gives an outline of living with haemophilia during the 1980's and 1990's.

 Mary Hanney is the mother of 2 boys, Sean aged 13 and Daniel aged 9, both have severe haemophilia A. Mary tells her story.


What is Haemophilia? Haemophilia is a lifelong bleeding disorder affecting mostly males which if left untreated can cause severe deformity, crippling and even death. Effective treatment has only become gradually available in the last 40 years in Ireland. These are the personal stories of 5 people and how their lives have been impacted by haemophilia over the last 4 decades. It is both touching and insightful, and chronicles how life has changed for the better through advancements in treatment and the tenacity of those demanding the best treatment and facilities.

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haemophilia through the generations

Personal Stories of Living with Haemophilia



IRISH HAEMOPHILIA SOCIETY

As IHS Production
Produced by: Shay Farrell, Margaret Dunne & Brian O'Mahony

Haemophilia through the Generations

DVD



National Haemophilia Program...Organisation

- National Haemophilia program with Government support
- Integrated within healthcare system
- National Register
- National treatment protocols
- Organised network of treatment centre's
- National purchase of replacement therapy



Organisation

- National Register at NCHCD
- IT system (Clintech) linking 3 comprehensive care centre's
- National Treatment protocols –NHC- endorsed by Irish Haematology Society
- 3 Comprehensive care centres- NCHCD /OLCH / CUH
- Secondary centres- Waterford /Galway / Limerick / Letterkenny / Sligo



NCHCD Ireland





Organisation

- National centre's offer 24 hour advice to other hospitals
- Patients self treat at home and attend centres for review /major bleeds / surgery/ HIV, Hepatitis C / Specialist care
- Statutory National Haemophilia Council
- Haemophilia Product Selection and Monitoring



Haemophilia Legislation- Ireland



Number 15 of 1996

HEALTH (AMENDMENT) ACT, 1996

ARRANGEMENT OF SECTIONS

Section

1. Short title, collective citation, construction and commencement.
2. Provision of health services without charge to certain persons who have contracted hepatitis C.



Number 34 of 1997

HEPATITIS C COMPENSATION TRIBUNAL ACT, 1997

ARRANGEMENT OF SECTIONS

Section

1. Interpretation.
2. Establishment day.
3. The Tribunal.
4. Claims before Tribunal.
5. Awards of Tribunal.
6. Disposal of and claims before non-statutory scheme Tribunal.
7. Regulations to give effect to Act.
8. Settlements.
9. Extension by regulations of persons who may make a claim before Tribunal.
10. Special account.
11. Reparation Fund.
12. Report of Tribunal.
13. Power to remove difficulties.



Number 21 of 2002

HEPATITIS C COMPENSATION TRIBUNAL (AMENDMENT) ACT, 2002

ARRANGEMENT OF SECTIONS

Section

1. Interpretation

SI No. of 2007

HAEMOPHILIA PRODUCT SELECTION AND MONITORING ADVISORY BOARD (ESTABLISHMENT) ORDER, 2007

I, Mary Harney, Minister for Health and Children, (herein referred to as "the Minister") in exercise of the powers conferred on me by Section 3 of the Health (Corporate Bodies) Act, 1961 (No. 27 of 1961) as amended by Section 22 of the Health (Amendment) (No. 3) Act, 1996 (No. 32 of 1996) and adapted by the Health (Alteration of Name of Department and Title of Minister) Order 1997 (S.I. No. 308 of 1997) hereby order as follows:

1. This Order may be cited as the Haemophilia Product Selection and Monitoring Advisory Board (Establishment) Order 2007.

2. In this Order:

"Board" means the Haemophilia Product Selection and Monitoring Advisory Board established by this Order;

"Chairperson" means the Chairperson for the time being of the Board;

"I" means the Irish Blood Transfusion Service, which is the body The Blood Transfusion Service Board (Establishment) Order, 1965 (S.I. or such other body as the Minister may establish or authorise;

"inherited" means the following disorders: inhibitors to factors VIII and IX, inherited factors I, II, V, VII, VIII, IX, X, XI, XII and Von Willebrand's Disease;

"means" means health services provided under the Health Acts 1947 to 2004 Treatment Acts 1945 to 2001;

"Executive" means the body established under Section 6 of the Health

is the Minister for Health and Children;

an employee of the Board, unless the context otherwise requires;

any clotting factor concentrate or concentrates used in the treatment of

3. (1) A body to be known as the Haemophilia Product Selection and Monitoring Advisory Board is hereby established to perform the functions conferred upon it by this Order.

Health (Amendment) Act Card

The authorised person is entitled to services under the Health (Amendment) Act, 1996.



National
Haemophilia
Council



GUIDE TO NATIONAL TENDERS FOR THE PURCHASE OF CLOTTING FACTOR CONCENTRATES



Brian O'Mahony

WORLD FEDERATION OF
HEMOPHILIA
FÉDÉRATION MONDIALE DE L'HEMOPHILIE
FEDERACIÓN MUNDIAL DE HEMOFILIA



| Score Sheet: Product Selection & Monitoring Advisory Group | | | FACTOR VIII (July 2008) | | | | |
|--|---|-----------------------|-------------------------|--|--|--|--|
| SCORING CRITERIA | | Total Marks Available | SCORES AWARDED | | | | |
| | | | | | | | |
| Phase 1 | | | | | | | |
| Safety | Human albumin in culture medium | 10 | | | | | |
| | Additional human or animal protein (eg monoclonal antibodies) | 5 | | | | | |
| | Viral inactivation | 10 | | | | | |
| | Inhibitors | 30 | | | | | |
| | Prion Removal | 10 | | | | | |
| | Excipients (presence or absence of albumin as a stabiliser) | 20 | | | | | |
| | Others | 10 | | | | | |
| | Total for Safety | 95 | | | | | |
| Efficacy | Recovery/Half Life (adult/paediatric) | 12 | | | | | |
| | Clinical Response (adult/paediatric) | 18 | | | | | |
| | Total for Efficacy | 30 | | | | | |
| Quality | Stability | 5 | | | | | |
| | Volume of Administration | 3 | | | | | |
| | Instructions for Use & Handling | 3 | | | | | |
| | Ease of Administration | 4 | | | | | |
| | Application of Unique Bar-Code | 3 | | | | | |
| | Total for Quality | 18 | | | | | |
| Security of Supply / Availability | Number of Manufacturing Plants | 6 | | | | | |
| | Security of Supply | 10 | | | | | |
| | Total for Supply/ Availability | 16 | | | | | |
| Scientific Support | Clinical Opinion | 3 | | | | | |
| | Consumer Opinion | 3 | | | | | |
| | Tender | 3 | | | | | |
| | Total for Scientific Support | 9 | | | | | |
| Total Scores Awarded: Phase 1 | | 168 | | | | | |
| Phase 2 | | | | | | | |
| Cost | Total For Cost | 30 | | | | | |
| Total Scores Awarded: Phase 2 | | | | | | | |