Regulations of the PedNet Haemophilia Research Foundation and the PedNet Haemophilia Registry

Additional to the articles nos. 1-16 of the Articles of Association of the PedNet Haemophilia Research Foundation (attached).

Version 3.1

Article 1 – Terminology and role descriptions

PedNet Haemophilia Research Foundation ("PedNet"): A foundation that coordinates an independent, international collaboration framework consisting of health centres and physicians treating haemophilia and allied disorders which is used as a forum to exchange experiences and to encourage international collaboration on paediatric care of haemophilia, to facilitate basic and clinical research endeavours specific to haemophilia and related coagulation disorders and to publish and present the results of such scientific research. PedNet is the legal body that coordinates the activities of the PedNet study group and manages the PedNet Haemophilia Registry.

PedNet study group ("PSG"): A study group consisting of physicians treating haemophilia and allied disorders where each Participating Centre is represented by one Representative.

Representative: A physician who treats haemophilia and allied disorders (Health Care Professional, "HCP") and who represents a Participating Centre.

Participating Centre: A treatment centre, admitted to the PedNet study group by the PedNet Board, where the Representative works and where he or she treats patients with haemophilia and allied disorders.

PedNet Haemophilia Registry ("PHR"): A database owned and administered by PedNet containing coded data of all children with haemophilia born from 2000-01-01 onwards, who are treated at one of the Participating Centres. PHR records and makes available a data collection for Participating Centres. The PHR data base is physically located at the University Medical Centre Utrecht (UMCU).

The Management Board of the Haemophilia Research Foundation ("PedNet Board"): The management board of PedNet which has the power of management of and represents PedNet.

Executive Director of the PedNet Haemophilia Research Foundation ("PedNet Director"): Is employed by PedNet, appointed by and reports to the PedNet Board and is responsible for execution of administrative matters of PedNet such as the infrastructure of the database, preparation and negotiations of legal and economic matters, oversight coordination of PHR studies, day-to-day matters, contact point for requesting information on Data and Data access conditions, and supervisor of the staff of PedNet. The PedNet Director is also appointed as "Data protection supervisor" and responsible for the protection of the Data in accordance with applicable regulations. The PedNet Board determines the details of the job description of the position.

Senior Study Coordinator of the PedNet Haemophilia Registry ("Senior Coordinator"): Is employed and appointed by PedNet and reports to the PedNet Board and on daily matters to the PedNet Director. The Senior Coordinator is responsible for the recruitment of all eligible patients in the Participating Centres and education of the physicians and nurses in the Participating Centres. The PedNet Director determines the details of the job description of the position.

Scientific Advisory Council: consists of seven Representatives who will be chosen by and among the Representatives and is tasked with setting up the rules for authorship, supervision and advising on new protocols and assisting the PedNet Board with scientific advice on annual research program, manuscripts and new participating centres. The Scientific Advisory Council will internally elect a chairperson. A member of the Scientific Advisory Council may not be a member of the PedNet Board at the same time.

Data: Coded information of data, according to the PedNet protocol, in the PHR on patients with congenital haemophilia A and B collected by the Participating Centres or in the course of a PHR Study.

PedNet Research Program: A multi-year research program of ongoing and planned PHR Studies, compiled by the PedNet Director and established by the PedNet Board after advice from the Scientific Advisory Council.

PedNet Protocol: A document which contains a detailed description of the PedNet Haemophilia Registry (PHR).

PHR Study: A study, approved by the PedNet Board after advice from the Scientific Advisory Council, based on data from the PHR.

Sponsor: a third party, being a pharmaceutical company or other interested party, that financially supports PedNet.

Article 2: PedNet Board - Organization and Tasks

1. The PHR is governed by the PedNet Board, consisting of an uneven number of at least three (3) members and no more than seven (7) members chosen from the Representatives. Such members are elected for a period of three years in accordance with PedNet's Articles of Association. A member of the board can be directly re-elected for a new 3-year period. Re-election is limited to one time.

2. The PedNet Board will appoint a PedNet Director to execute the tasks as indicated in Article 1.

3. The PedNet Board is responsible for the settlement, spending and receiving of the annual budget of PedNet.

4. The PedNet Board will report annually to the Participating Centres and the PedNet sponsors ("Annual Report").

5. After formal application by a Participating Centre, the PedNet Board will decide on approval of proposals for studies using Data of the PHR. Data may not be used without such permission from the PedNet Board.

6. The PedNet Board will approve the PedNet Protocol and the PedNet Research Program or amendments of the PedNet Research Program and PHR Studies.

7. The PedNet Board will also decide on the following subjects:
   - Organisation of the Data collection (IT-infrastructure)
   - Content of the PHR
   - Permission to submit manuscripts of PHR Study results
   - Payment to the Participating Centres for collecting data
   - Admission of new Participating Centres in PedNet (invitation and dismissal)

8. The PedNet Board endeavours to have a minimum of one face-to-face meeting per year and regular telephone conferences at least once every three months or at the reasonable demand of a Participating Centre. The Chairperson of the Scientific Advisory Council will be invited to the annual face-to-face PedNet Board meeting.

9. More details regulating the PedNet Management Board (PedNet Board) can be found in the Articles of Association ('Statuten') of the PedNet Haemophilia Research Foundation:

   - The constitution and operation of the PedNet Board is arranged for in article 4.

   - The PedNet Board meetings and resolutions are arranged for in in article 5.

   - The powers of the PedNet Board and representation are arranged for in in article 6 and article 7.

- The termination of PedNet Board membership is arranged for in article 8.

- The constitution and operation of the PedNet study group is arranged for in article 10.

- The constitution and operation of the Scientific Advisory Council is arranged for in article 11.

Article 3: Participation in the PedNet study group

1. A haemophilia treatment centre that may be invited to participate in the PSG as a Participating Centre by the PedNet Board if it fulfils the following criteria:

   - Centres should be recognized by EUHANET as European Haemophilia Comprehensive Care Centres (EHCCCs)
   - Centres need to care for children with haemophilia and have preferable a paediatrician or paediatric haematologist
   - Centres need at least to include 2 or more new severe haemophilia patients per year (calculated over a 3-5 year period)

2. A Representative ends their position in the PedNet study group:
   a. When the Representative stops working at a Participating Centre;
   b. By decision of the PedNet Board.

3. Representatives meet annually at the annual PedNet Haemophilia Research Foundation meeting.

4. The PedNet study group nominates (non-binding) members to replace vacancies in the PedNet Board.

5. Representatives agree to collect Data, according to the PedNet protocol, from patients with congenital haemophilia A and B (severe, moderate and mild, factor VIII or IX up to 25%) born from January 1st 2000 onwards. The Participating Centres and Representatives agree to participate in quality control of data according to the Monitoring Plan.

6. Participating Centres will receive a patient fee for reported patients. PedNet's and Participating Centres' obligations and rights will be arranged in consortium agreement(s) with PedNet as legal representative of the PedNet Registry and the Participating Centre in question, a model of which is attached here to as Annex A.

Article 4: Data: collection, ownership, use and publication

1. Data will be collected under the responsibility of the Representatives in each of the Participating Centres in accordance with the PedNet Protocol, the written instructions of the PedNet Board and all applicable laws, regulations and procedures at the time of Data collection initiation, including but not limited to

the General Data Protection Regulation (GDPR) and applicable national implementation legislation.

2. Representatives, researchers and other staff employed by a Participating Centre for the execution of a PHR Study have to sign a confidentiality statement before they are allowed to use data for analysis.

3. The data which are entered into the PHR by the Participating Centres shall remain the property of the Participating Centres and no use will be made of them other than for the purpose stated in the PedNet Research Program.

4. Use of the Data collection is limited to Participating Centres. The PHR will be used for scientific research. Each study using the Data in the PHR has to be approved by the PedNet board with the advice of the Scientific Advisory Council.

5. All results and any inventions or discoveries made as a result of a PHR Study will be the property of PedNet.

Article 5: Funding and Sponsorship

PedNet may be financially supported by third parties, including pharmaceutical companies. Sponsorship benefits are limited to receipt of aggregated anonymous data concerning the Sponsor's products. All Sponsorship shall be provided on the basis of a written agreement, a model of which is attached hereto as Annex B.

All Sponsorship shall be fully transparent and public. The identity of Sponsors and the Sponsorship amounts shall be registered in the public Dutch Transparency Register Health. PedNet remains ownership of the information shared with its Sponsors at all times.

Requests for Sponsorship shall be managed and negotiated by the PedNet Director and approved by the PedNet Board.

Sponsors shall be acknowledged for their support of PedNet/PHR in publications.

PedNet, PHR and satellite studies can be funded by:
- Industry Grants;
- Regular research grants;
- Subsidies;
- Gifts and legacies.

Funding shall be unrestricted.

Article 6: Termination

Termination of the PedNet Haemophilia Research Foundation is arranged for in article 15 of the of the Articles of Association ('Statuten') of PedNet. The future ownership or

cancellation of the PHR has to be determined at the final meeting of the PedNet Board.

These regulations were accepted by the PedNet board on May 8th 2020 and by the members as final agreed at the PedNet annual meeting on September 11th 2020.

The English version of the articles of association ('Statuten') of the PedNet Haemophilia Research Foundation, established on December 16th 2016 is attached hereto as Annex C.

Annex A: Consortium agreement format
Annex B: Sponsorship agreement format
Annex C: Articles of association of the PedNet Haemophilia Research Foundation