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

GTR
WFH GENE THERAPY REGISTRY

WFH Gene Therapy Registry

User guide for hemophilia treatment centres

World Federation of Hemophilia
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The World Federation of Hemophilia (WFH) Gene Therapy Registry (GTR) welcomes the participation of all Hemophilia Treatment Centres (HTCs) involved in gene therapy. This includes HTCs that administer gene therapy and those that manage or follow-up with patients who have received gene therapy at other centres. This user guide will orient HTCs to the WFH GTR, outlining how HTCs can successfully participate in the registry.

Please reach out to WFH with questions regarding participation in the registry: **gtr@wfh.org**

This user guide provides information on implementing the WFH GTR at your HTC, including complying with all regulatory and protocol requirements, obtaining ethics approval, obtaining informed consent from participants, and entering data into the registry.

Gene Therapy Registry for Hemophilia: Key Players

Participating HTCs

- **Administering HTCs:** Centres that administer gene therapy treatments
- **Follow-up HTCs:** Centres that manage or follow patients that have received gene therapy

Participating people with hemophilia

- **People with hemophilia (PWH)** who have received gene therapy and have consented to be part of the registry

GTR Governance

The WFH GTR is governed by advisory boards composed of accomplished experts in the field of gene therapy, appointed by the World Federation of Hemophilia.

World Federation of Hemophilia

- **WFH GTR Steering Committee**

  The WFH GTR is governed by a multi-stakeholder steering committee composed of representatives from the International Society on Thrombosis and Homeostasis (ISTH); the National Hemophilia Foundation (NHF); the European Association for Haemophilia and Allied Disorders (EAHAD); the European Haemophilia Consortium (EHC); industry representatives; and people with hemophilia

- **WFH GTR Scientific Advisory Board**

  The WFH GTR Scientific Advisory Board, composed of a select group of members of the Steering Committee, will provide advice on all scientific questions relating to the WFH GTR and any data stemming from the WFH GTR

HTC Care Team

The HTC Care Team involved in the WFH GTR typically consists of:

- **Principal Investigator (PI):** Each HTC will designate one person as the PI for its institution. This individual will coordinate the administration of the WFH GTR at the institution level and be responsible for ensuring compliance with regulatory rules and protocol adherence.
- **Registry Data Coordinator/Manager:** Each HTC will designate one or more persons to coordinate the WFH GTR at its HTC. This role may include educating patients about the registry, participating in the informed consent process, and entering data into the registry. The WFH will provide one-on-one training on data entry. More than one person may be designated to enter data into the registry. However, we suggest limiting the number of people involved to ensure accuracy and data privacy.

Responsibilities of the HTC

Ethics approval

Participating HTCs will require approval by their individual Institutional Review Board (IRB) or Independent Ethics Committee (IEC) prior to participating in the WFH GTR. It is the responsibility of each HTC to obtain and maintain ethics board approval. However, the WFH will provide guidance and necessary information for submission documents or specific country requirements.

SCAN QR CODE to access the documents listed below, provided by the WFH

- **WFH GTR Patient Informed Consent Form:** This consent form template is used to obtain written consent from all patients participating in the registry
- **Patient Information Sheet:** A customizable patient-facing document that orients patients to the registry with a FAQ and definition of terms
- **Patient Engagement Form:** A patient form reinforcing the importance and benefits of long-term follow-up within the registry. This form is optional, but highly recommended.
- **WFH GTR Protocol:** A detailed description of the objectives, study design, data management, and registry governance
- **Core Data Set:** A detailed list of the data and response fields of the WFH GTR
- **Data Privacy and Security Documents:** Information describing data privacy and security guidelines for HTCs participating in the WFH GTR

After IRB or IEC approval, HTCs are responsible for ensuring compliance and maintenance of approval by submitting updates to the ethics board as required by their institution, state, or country. A copy of all approval documents, original or updated, should be sent to the WFH. If you have any questions through the ethics approval process, please email gtr@wfh.org.

Patient recruitment

Participating HTCs will invite all eligible patients to participate in the registry. Optimally, recruitment will occur when patients and their medical team decide to proceed with gene therapy. Joining the registry before therapy will aid in the collection of required baseline information.

However, HTCs can recruit patients anytime after gene therapy. The WFH will provide the **WFH Patient Information Sheet** and **WFH GTR Participant Informed Consent Form** to help introduce the registry to patients and obtain their consent. The HTC health care team will help participants understand the material, answer all questions, and obtain consent to participate in the registry. It is essential to help patients understand the importance of long-term follow-up for gene therapy recipients.

Obtaining informed consent

- **WFH GTR Patient Informed Consent Form**

  The WHF GTR informed consent form complies with the International Council for Harmonisation (ICH) consent checklist and guidelines[1]. If information arises that may influence the patient's willingness to continue participation in the registry, the WFH will update the consent form and inform HTCs of the changes. Key factors of the consent form include:

  - The purpose of the registry
  - A statement regarding the use of data
  - Responsibilities of participants
  - Benefits and risks of participation
  - Information regarding voluntary participation
  - Expected duration of participation
  - Contact information for HTC

[1] ICH Harmonized Guideline. Integrated addendum to ICH E6 (R1): guideline for good clinical practice E6 (R2).2015 Current Step.;2:1-60.

Best practice

It is important to follow good clinical practice when obtaining informed consent from participants, as outlined in the ICH guidelines.

Selected principles of best practice are:

- Fully inform patients about the benefits and risks of participating in the registry
- Help patients understand that their participation or non-participation in the registry will not affect the treatment and care they receive at the HTC
- Use non-technical language, at an 8th-grade reading level or lower, to ensure patients fully understand
- Translate the consent form into native languages. All translated versions must be approved by the ethics board.
- Help patients understand that participation is voluntary, and they can withdraw from participation at any time, for any reason
- If a patient cannot read, a witness should be present during the consenting process
- Provide time for the patient to review the consent document and ask questions
- Avoid coercion or undue influence
- Use the **WFH GTR Patient Informed Consent Form**
- Give the patient a copy of the signed and dated informed consent form

Data Entry

Training

The WFH team will provide required virtual training for the principal investigator, physicians, and data coordinators/managers on data entry and the use of the WFH GTR.

After initial training, additional training can be requested for new staff, or the WFH team may require additional training if the registry changes.

In addition, the WFH team will supply the HTC with supporting documents. **SCAN QR CODE** to access. You may contact the WFH team with questions at any time.

Data entry schedule

HTCs will collect data at regularly scheduled visits.

Demographic, diagnostic, and medical history data will be collected from the patient chart at the pre-treatment visit (baseline) after signed informed consent. Data on vector infusion will be collected at the treatment visit. Clinical and treatment data will be collected quarterly for the first year post-treatment, semi-annually during the second year, and annually throughout the patient's lifetime. Details regarding data collection and entry can be found in the **Data Entry Guidelines Document**. In general, the recommended data entry schedule follows the **WFH GTR Protocol** as listed below:

Assessments	Screening	Baseline	Treatment Day	Month 3	Month 6	Month 9	Month 12	Month 18	Annually
Historical data									
Hemophilia details	x								
Demographics		x							
Diagnostic details		x							
Medical, clinical history		x							
Treatment									
Vector infusion details			x						
Safety									
Adverse drug reactions			x	x	x	x	x	x	x
Adverse Events (AEs), AEs of special interest*			x	x	x	x	x	x	x
New onset of comorbidities			x	x	x	x	x	x	x
Elevated liver transaminases			x	x	x	x	x	x	x
Inhibitor testing			x	x	x	x	x	x	x
Efficacy									
Bleeding requiring treatment				x	x	x	x	x	x
Factor level testing		x		x	x	x	x	x	x
Use of factor or non-factor treatments				x	x	x	x	x	x
Surgery									
Bleeding requiring treatment				x	x	x	x	x	x
Quality of Life									
EQ-5D-5L		x			x		x		x
PROBE		x			x		x		x
Mortality									
Death		x	x	x	x	x	x	x	x

Safety and adverse events

The primary obligation of reporting individual safety events is with the treating physician.

HTC staff should inquire about safety events at each patient visit. HTCs are responsible for entering Serious Adverse Events (SAEs) and events of special interest (EOSI) into the WFH GTR database. Entering an adverse event in the WFH GTR database will trigger a notification to the HTC to ensure this adverse event is also reported through their official channels.

*Adverse events of special interest include:

- FVIII inhibitors
- FIX inhibitors
- Thromboembolic events
- Autoimmune disorders
- Malignancies
- Liver disease
- Sensory paresthesias
- Hypersensitivity reaction
- Hepatitis B (new or reactivation)
- Hepatitis C (new or reactivation)

SCAN QR CODE to refer to the **WFH GTR Protocol**

Data quality program

The WFH GTR includes a comprehensive data quality program. The WFH may contact registry data coordinators/managers at HTCs with requests to supply or correct data in the registry or to participate in an audit.

Source document validation, through a combination of on-site and electronic source document transfer, will be conducted.

Retaining registry participants over time

Retention of participants in the registry is crucial to determining the gene therapy's long-term safety and efficacy.

HTCs can improve the retention of patients by establishing clear lines of communication with their participants and facilitating a relationship of trust between the care team and participants. Regular contact, reminders, and problem solving with the participant regarding their barriers can help increase their participation time in the registry. Because the primary purpose of the database is to identify any long-term safety risks of gene therapy, it is imperative to help participants understand the importance of their lifetime yearly visits.

The GTR is supported by funding from:

FOUNDING VISIONARY PARTNERS

BIOMARIN

CSL Behring
Biotherapies for Life™

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