ERN eUROGEN registry
Data Access and Sharing Policy

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ERN eUROGEN registry Project Leader	*Wout Feitz (wout.feitz@radboudumc.nl)*
ERN eUROGEN registry Coordinator	*Loes van der Zanden (loes.vanderzanden@radboudumc.nl)*
ERN eUROGEN registry Manager	*Lotte Boormans (lotte.boormans@radboudumc.nl)*
ERN eUROGEN registry Developer	*Isabel Hageman (isabel.hageman@radboudumc.nl)*
ERN eUROGEN registry Quality Coordinator	*Wim Witjes (wim.witjes@radboudumc.nl)*
ERN eUROGEN registry Central Monitor	*tbd*
Project Steering Committee (PSC)	*Wout Feitz (wout.feitz@radboudumc.nl)* *Loes van der Zanden (loes.vanderzanden@radboudumc.nl)* *Darren Shilhan (darren.shilhan@radboudumc.nl)* *Wim Witjes (wim.witjes@radboudumc.nl)*
Advisory Board (AB)	*Jorgen Thorup (joergen.mogens.thorup@regionh.dk)* *Kate Abrahamsson (kate.abrahamsson@vgregion.se)* *Vijay Sangar (vijay.sangar@nhs.net)* *Dalia Aminoff (dalia.aminoff@gmail.com)* *Nicole Schwarzer (info@soma-ev.de)*

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LIST OF ABBREVIATIONS AND RELEVANT DEFINITIONS

AB Advisory Board
DTA Data Transfer Agreement
ERN European Reference Network
HCP Health Care Provider
PSC Project Steering Committee

1. INTRODUCTION

European Reference Networks (ERNs) are virtual networks gathering doctors and researchers with high expertise in the fields of rare or low-prevalence and complex diseases. ERN eUROGEN is the ERN for rare urogenital diseases and complex conditions. Present registries in the field of rare urogenital diseases lack uniformity. ERN eUROGEN wants to facilitate knowledge sharing and improved coordination of care through the continuous and comprehensive collection of relevant patient information. Therefore, a large population registry on rare urogenital diseases and complex conditions, the ERN eUROGEN registry, is a top priority.
This registry will comprise different elements:

- The Common Data Elements.
- A Clinical Practice Snapshot containing 6 disease-specific questions about the clinical procedures performed for disease areas 1.5 posterior urethral valves, 1.7 anorectal malformations, 1.8 pediatric kidney transplantations, 2.1 complicated pelvic floor disorders, and 3.3 adrenal tumors. Clinical Practice Snapshots for the other disease areas are under development.
- Data elements on the follow-up of patients will be added to the registry in due time. The data elements to be collected and the timing of collecting them will be defined by experts in the field.

The ERN eUROGEN registry consists of both a retrospective and a prospective part.

- In the retrospective part, Health Care Providers (HCPs) involved in ERN eUROGEN as a Full Member or Associated National Centre and recognised as a centre of expertise for 1 or more of the 5 disease areas for which the Clinical Practice Snapshots were developed will retrospectively include their last ~30 patients with diseases from these disease areas.
- In the prospective part, all patients presenting with a rare urogenital disease or complex condition at a HCP that implemented the ERN eUROGEN registry will be asked for informed consent to have their data entered in the ERN eUROGEN registry.

2. ROLE BASED ACCESS RULES

The ERN eUROGEN registry will be implemented in Castor using a Data Processing Agreement between the Radboudumc and Castor. Only HCPs who signed the Collaboration Agreement will obtain access to the online registry. Access of authorized users to the online registry is controlled by assignment of a secure, individualized password. A hierarchical access authorization system has been developed:
The Project Steering Committee (PSC) members and Project Leader will have management rights and be able to:

- Manage Forms: View and edit study structure and forms
- Manage Users: Add users and manage their rights
- Manage Settings: View and edit study settings

All online registry users will be able to:

- Manage Records: Access record overview and study statistics

In addition, there are several rights that give the ability to add, edit and view data. The rights that will be used for users of the ERN eUROGEN registry are (see table below for specification of rights per role and centre):

- Add: Add new records or reports
- View: View existing records
- Edit: Add and edit data, add comments, and respond to queries
- Query: Create queries and close them upon resolution
- Email: See and modify the email addresses of participants
- Send surveys: Send out surveys to participants
- View surveys: View answers to surveys filled out by participants
- Export: Export data
- Sign: Sign completed forms -> If data in a form is changed after the form was signed, the signee will be notified
- Lock: Lock records to prevent further changes
- Archive: Archive unnecessary records

User description	Rights for own HCP	Rights for all HCPs
Coordinator*	-	View, query, send & view surveys, export
Manager*	-	View, query, send & view surveys, export
Central Monitor*	-	View, query, lock
Principal Investigator*	Add, view, edit, query, email, export, sign, archive	
Data Manager*	Add, view, edit, email	-

** See ERN eUROGEN registry Protocol for an explanation of the different roles*

3. OWNERSHIP OF THE DATA

In the ERN eUROGEN registry, the patient participant (the 'data subject') is the primary owner of the data and will give consent to use such data for research and other purposes. In case the patient participant is under the age of majority, or subject physically or legally incapable of giving consent, parent(s) or legal representative(s), is/are the primary owner(s) of the data and will grant the consent to use such data for research and other purposes. The Radboudumc is the current owner of the ERN eUROGEN registry platforms. The HCP of the clinician participant who has entered the data is responsible for the data of that patient participant and acts as the 'data controller' at the local centre. For all data submitted to the central registry database, the Radboudumc and its principal investigator Prof. dr. Wout F.J. Feitz is responsible for the protection of the data, its storage, use and access. When processed, the data become research data and are then the intellectual property of the investigator who is the 'third party'. This third party has to abide by the agreement reached in the Data Sharing Agreement whilst using the data supplied for the purpose stated in de Data Request form.

4. ANTICIPATED DATA ANALYSES

Several analyses are anticipated for:

- The PSC will keep track of the progress of data entry by the different HCPs. For the retrospective part of the ERN eUROGEN registry, this means they will notify HCPs that did not deliver data of their last ~30 patients within the given deadline. For the prospective part of the ERN eUROGEN registry, the PSC will perform analyses on the amount of data entered by the different HCPs every 6 months, and provide the HCPs with progress reports.
- The PSC will assign a Central Monitor who will analyse the data in the ERN eUROGEN registry at regular intervals, producing detailed data consistency evaluations. These analyses will focus on overall data accrual, content and quality and will be performed with the oversight of, and in close collaboration with, the PSC.
- To generate fast results on the diagnostic and treatment procedures at the HCPs across Europe, the retrospective part of the ERN eUROGEN registry will be analysed when data collection for this part is complete or when enough data are available, according to the procedures described below.
- All other analyses, such as analyses to monitor treatment performance or patient outcomes, or analyses to identify contemporary cohorts of patients with a certain condition for clinical research, are not planned yet and can only be carried out under the conditions set out below.

5. PLANNED ANALYSES OF DIAGNOSTIC AND TREATMENT PROCEDURES

5.1. Aim of the data analyses

The retrospective part of the ERN eUROGEN registry will be analysed when all HCPs involved have entered the data of the patients who provided Informed Consent. These analyses will be performed for the 5 selected disease areas and will provide insight into both the numbers of patients treated at the different HCPs and the differences in diagnostic and treatment procedures among different HCPs across Europe. It will enable generation of statistics for the whole of Europe, or separately by HCP or by country, about:

- the number of patients with specific forms of the conditions,
- the moment of onset of symptoms,
- the moment of diagnosis,
- the moment of treatment,
- the treatment procedures performed, and
- the number of direct complications arising from these procedures.

5.2. Sharing of the data

- Scientific Researchers who are associated with an HCP that entered data into the ERN eUROGEN Clinical Practice Snapshot for a disease area, are invited to apply for the task of analyzing the ERN eUROGEN registry for that disease area.
  - If nobody applies for a disease area, the PSC will assign a Scientific Researcher to perform this task.
  - If multiple Scientific Researchers apply for the same disease area, the PSC will, together with the Advisory Board (AB, consisting of 3 ERN eUROGEN representatives and 2 European patient advisory group (ePAG) representatives), decide which Scientific Researcher is best qualified to perform the task as leader of the group. All of those who showed interest and applied for a specific disease area will be involved in the analyses. An inclusive approach will be followed and all involved should agree upon the results, conclusions and recommendations or state specific differences in views.
- Names of all Scientific Researchers involved in the analyses will be published on the ERN eUROGEN website.
- A Data Transfer Agreement (DTA, see Annex 1) will be drawn up and signed by the Scientific Researcher (group leader) and the Project Leader or all members of the PSC.
- The ERN eUROGEN registry Manager or Coordinator will provide the data from the ERN eUROGEN registry anonymously or in encrypted form (pseudonymised) using the SPIDER Tool provided by the EU (when available) or follow up systems.

5.3. Analyses of the data

The Scientific Researcher will perform analyses and generate statistics for the total cohort, statistics stratified per HCP, and statistics stratified per specific diagnosis, phenotype, genetic diagnosis, and/or subtype of the condition. These statistics will entail the number of observations and averages or medians with a measure of spread such as standard deviation or interquartile range but not the total range. Results will be generated on:

- The number of male, female, undetermined and foetus patients.
- The age of patients at onset of symptoms.
- The age of patients at first contact with the HCP.
- The time between onset of symptoms and first contact with the HCP.
- The age of patients at diagnosis.
- The time between onset of symptoms and diagnosis.
- The time between first contact with the HCP and diagnosis.
- The number of patients with specific diagnoses, phenotypes, genetic diagnoses and subtypes of the condition
- The number of patients that received the different treatment procedures.
- The age of patients at the different treatment procedures.
- The time between onset of symptoms and the different treatment procedures.
- The time between first contact with the HCP and the different treatment procedures.
- The time between diagnosis and the different treatment procedures.
- The number of patients with the characteristics, complications, problems and/or results asked for in the ERN eUROGEN registry (left and right presence of vesicourethral reflux, grade of vesicourethral reflux, constipation and treatment, incontinence and severity, underlying disease, previous therapy or treatment, etc).
- The values of results asked for in the ERN eUROGEN registry (left and right renal function, grade of vesicourethral reflux, lowest creatinine values, number of HLA mismatches, etc).
- The number of patients who died.
- The age at end of follow-up.
- The age at death, if applicable.
- The time between onset of symptoms and end of follow-up.
- The time between onset of symptoms and death, if applicable.
- The time between first contact with the HCP and end of follow-up.
- The time between first contact with the HCP and death, if applicable.
- The time between diagnosis and end of follow-up.
- The time between diagnosis and death, if applicable.
- The time between the first treatment procedure and end of follow-up.
- The time between the first treatment procedure and death, if applicable.

6. OTHER ANALYSES USING DATA FROM THE ERN EUROGEN REGISTRY

Scientific Researchers, clinicians, patient organisations, policy makers, companies, etc. (all referred to as "Applicant" below) are invited to apply for utilisation of the data from the ERN eUROGEN registry. The following conditions must be met before personal data can be used for research or sent to new cooperation partners:

- An application form (Annex 2) must be completed and approved by the ERN eUROGEN registry Data Access Committee (consisting of the PSC and the AB). The ERN eUROGEN registry Data Access Committee will treat the applications confidentially and decide whether the planned research can be facilitated based on:
  - Compliance with the ethical approval that was obtained for the ERN eUROGEN registry.
  - Availability of sufficient personal data for the research.
  - Scientific quality of the planned research: The research protocol must describe the research objective and research question in a clear, concrete, brief and succinct manner. The research question must clearly describe to what extent and in what way this research will contribute towards a better insight into / knowledge about the conditions (in other words, what is the added value of this research). The approach and methodology must be clearly and logically described. The protocol must contain a chronological plan of the chosen methods/analyses, detailing why this approach was chosen.
  - Relevance of the planned research: The research protocol must meet the objectives of the ERN eUROGEN registry. The research must meet societal needs and must be in the interest of the patient or clinician.
  - Qualification of the Applicant and feasibility of the planned research: regarding the research protocol, it must be plausible that it can be achieved within the scheduled time period, using the expertise, manpower, finance and facilities that are available. It must describe any possible positive and negative factors. The researcher is responsible for execution of the research as it is described in the research protocol and within the described period.
  - Overlap with other planned, ongoing, or finalized research projects.
  - Data protection and security issues.
  - Acknowledgement of contributors of the ERN eUROGEN registry via co-authorships or otherwise.
- The ERN eUROGEN registry Data Access Committee has the option of making 3 different decisions:
  - To approve the research protocol.
  - To give conditional approval on the condition that … The ERN eUROGEN registry Data Access Committee will then make a proposal to modify the research protocol, after which the protocol may be resubmitted and a new decision will be made.
  - To reject the research protocol on the grounds of scientific or ethical reasons. These reasons will be communicated to the researcher.
- Approval can be achieved only with the full agreement of each party, meaning that nobody may object to the application and that, in absence of all members, at least one member of each party (one member of the PSC, an ERN eUROGEN representative from the AB and a patient representative from the AB) has to agree. The optimal research set-up will be worked out in consultation.
  - After approval by the ERN eUROGEN registry Data Access Committee, the PSC will inform the ERN eUROGEN registry Principal Investigator of each of the HCPs whose data were requested about the planned data sharing via e-mail. These persons have 2 weeks to object to the planned data sharing. If they do not object within these 2 weeks, data from patients entered by their HCP will be shared.
- After approval, a DTA (see Annex 1) Is drawn up and signed by the Applicant and the a member of the PSC. This DTA will contain at least the items mentioned in paragraph 4.2.
- The approved data provision will be published on the ERN eUROGEN website.
- The PSC will provide the data from the ERN eUROGEN registry anonymously or in encrypted form (pseudonymised) using the SPIDER Tool provided by the EU (when available) or follow up systems.

7. PUBLICATION OF THE RESULTS

Scientific Researchers and Applicants are entitled to publish the research results (both 'negative' and 'positive'), resulting from research that has been carried out with personal data from the ERN eUROGEN registry and, at the same time, have a duty to publish within a reasonable period of time. Any deviations from this are possible only if based on well-founded objections. Changes to the publication plans will be discussed with the PSC. Depending on the agreements regarding copyright, the institution or the author(s) of an intended publication on the research results is the owner of the manuscript.

- The Scientific Researcher or Applicant will publish the results in peer-reviewed scientific journals or, if this is not possible, make the research results public by other means. For example, by mentioning them on publicly accessible websites or in a presentation during scientific meetings.
- The Scientific Researcher or Applicant will send a copy of all publications and presentations to the ERN eUROGEN Secretariat for the ERN eUROGEN Monitoring reporting and validation process.
- The Scientific Researcher or Applicant will provide the PSC with a final report of the results, whether patentable or not.
- The PSC will forward the results to the HCPs whose data were used. These parties will obtain a free-of-charge and non-exclusive license to use the results for ERN eUROGEN-related clinical, research and educational purposes.
- The PSC will publish results that can be published on the ERN eUROGEN website.
- The Scientific Researcher or Applicant will destroy the data export that he/she received from the HCP 5 years after publication of the results.

All publications resulting from research carried out using personal data that have been made available by or on behalf of the ERN eUROGEN registry should acknowledge the ERN eUROGEN registry with a disclaimer:

"The data used in this project were provided by the ERN eUROGEN registry, funded by the European Union's Health Programme (2014-2020). The content of this [*insert appropriate description, e.g., report, publication, conference, etc.*] represents the views of the author only and is his/her sole responsibility; it cannot be considered to reflect the views of the ERN eUROGEN, the European Commission and/or the Consumers, Health, Agriculture and Food Executive Agency (CHAFEA) or any other body of the European Union. ERN eUROGEN, the European Commission and the Agency do not accept any responsibility for use that may be made of the information it contains."

Co-authorships on scientific publications emerging from ERN eUROGEN registry data will generally be granted based on the ICMJE criteria (www.icmje.org):

- Substantial contributions to the conception or design of the work; OR
    - the acquisition, analysis, or interpretation of data for the work; AND
- Drafting the work or revising it critically for important intellectual content; AND
- Final approval of the version to be published; AND
- Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Substantial contribution to the acquisition of data will mean that each HCP will be entitled to name 1 co-author for each publication that reports results generated from analyses of data that they have provided. These co-authors will be named under the umbrella group of the ERN eUROGEN HCPs. Other co-authors will be agreed upon before the data are shared in the DTA. The co-authors must be able to read the draft article/abstract at least once before it is submitted and provide comments within a reasonable period of time, which is 2 weeks for an article and 1 week for an abstract. If an author does not provide comments or approval within this timeframe, his/her name will be removed from the publication.

ANNEX 1: DRAFT DATA TRANSFER AGREEMENT

Please find the link to a draft DTA below:
https://elsi.health-ri.nl/sites/elsi/files/2020-07/Template%20-%20Data%20Sharing%20Agreement_werkversie.docx

ANNEX 2: APPLICATION FORM ERN EUROGEN REGISTRY

Title research protocol	
Name / title / function applicant	
Institute / department applicant	
Address applicant	
Tel / Fax / E-mail applicant	
Collaborating partners	
Relevant publications of the applicant for this project (max. 5)	
Summary research activities of the applicant (max. 2000 characters)	
Background / rationale research (including pilot study when applicable)	
Aim of the research / research question	
Work plan (including methodology)	
Expected benefit of the project	
Indication of the time schedule of the project	
Is there medical-ethical approval for the research project?	
Patient population (diagnoses, in- and exclusion criteria)	
Type of data needed to perform the research (data elements)	
Financial support for the project (government, company, grant, personal investment, etc)	
How will the results be published / reported?	
***Addition to be filled in by the** ERN eUROGEN registry Data Access Committee:*	
Suggested eUROGEN co-authors on publications	
Suggestion for text on website	

Date of handing in the application form:

http://eurogen-ern.eu/

Co-funded by the European Union

ERN eUROGEN is one of the 24 European Reference Networks (ERNs) approved by the ERN Board of Member States. The ERNs are co-funded by the European Commission. For more information about the ERNs and the EU health strategy, please visit http://ec.europa.eu/health/ern