



Data Access and Publication Rules for the ESID Online Database

ESID encourages the submission of research proposals from researchers interested in analyzing registry data. This document

- defines the data access rules, based on the regulations laid down in §2 of the Agreement between the European Society for Immunodeficiencies (ESID), and a Documenting Centre regarding the ESID Online Registry ("ESID Agreement", see Annex A).
- provides authors with guidelines for the ESID Registry research and publications process from submission of a research proposal to generation of a manuscript. We require that authors adhere to these guidelines when preparing proposals, abstracts, and manuscripts.

Rules for data access

As laid down in the ESID Agreement, each documenting centre remains the owner of all data it has entered in the ESID Database. This means that in principle, data entered by a documenting centre may not be used for analysis or publication unless the documenting centre has agreed to data access for a given, specified project. Exceptions are given below.

The ESID Agreement further specifies that data is made available to the sponsors of the ESID Database for internal purposes (given the patient's written consent). This currently applies to the PPTA. If PPTA wishes to publish data, it needs to obtain the written consent from the ESID registry steering committee to do so.

Furthermore, data can be made available to documenting (ESID) centres, PID researchers or epidemiologists. This implies the extraction of data by the ESID Database team and

- a) the transfer of this data from the ESID Database to a third party or
- b) the statistical evaluation of this data by the Database team and provision of the results to the third party.

Application for data access proceeds as follows:

1. A written request is addressed to the ESID registry steering committee (via the chairperson of the ESID registry working party, esid.registry@kenes.com).

The request shall contain:

- Title and description of the study (please use the Research Proposal form provided on the ESID website)
 - Supporting letter by the program director
 - Names and affiliations of the investigators
 - A disclosure statement regarding potential conflicts of interest (such as financial affiliations with pharmaceutical companies)
2. The ESID registry steering committee will then review the proposal according to the criteria outlined below. This will include a feasibility check by the registry team (Is the number of patients sufficient to address the question? Is data completeness sufficient?).
 3. If approved, the ESID registry team will perform a search for the relevant datasets and contact the centers that have contributed these data to obtain their approval to participate in the study.
 4. Data extraction and analysis will be supported by the registry team.

Evaluation criteria for registry research proposals (1 - 5 points each):

- Is the proposal within the scope of the ESID Database?
- Does this proposal address an important problem?
- Are the conceptual or clinical framework, design, methods, and analyses adequately developed, and appropriate to the aims of the proposal? Is the study feasible?
- Is the proposal original and innovative?
- Are the investigators appropriately trained and suited to carry out this work? Does the scientific environment in which the work will be done contribute to the probability of success? One of the investigators should be a recognized specialist in the subject.

Rules for statistical queries

Statistical queries are defined as requests by researchers asking for the number of patients with specific characteristics. Examples for such a query are:

How many of the DiGeorge patients registered in ESID have an autoimmune disease? How frequent is each of these (e.g. autoimmune cytopenia, vasculitis, arthritis)

How many patients are there with liver failure and cholangitis associated with cryptosporidia?

Such requests have been sent very frequently to the database coordination in the past. The purpose of these is either

- a) to check whether there are enough patients with the given characteristics to initiate a multi-centre study and submit a study proposal to the ESID Registry steering committee or
- b) to have reference values for some purpose (e.g. for internal discussions within a research group)

In these cases, it is not necessary to send a study proposal to the Registry team. However, the following rules must be observed:

(i) The query may involve **no more than two variables**. Examples for permissible queries are:

How many DiGeorge patients have had neoplasms?

Which percentage of CVID patients is on Ig replacement?

If there are more variables, a **study proposal must be submitted**. Examples for such queries are:

How many DiGeorge patients have had neoplasms and CD4<10%?

Which percentage of CVID patients is on Ig replacement and has splenomegaly?

(ii) only **summarizing, aggregated data** is transmitted to the requesting person. This means that **no per-patient** data and **no per-centre** data is transmitted.

(iii) the results are **not published**. If the requesting person intends to publish the results, he must adhere to **rule 3 of the publication rules** ("3.Data from the registry are evaluated, but make a minor point in a larger paper"). This also applies if the data is presented at a public meeting (e.g. scientific conference or health-care meeting).

Rules for publication

1. Publication of statistics without prior notice to the documenting centres

Statistics on the following items are regularly published on the ESID Website and in ESID Newsletters:

- Total number of patients
- Prevalence of PID per country
- Number of patients by main category
- Number of patients by centre
- Number of living patients receiving Ig-replacement (intravenous, subcutaneous, intramuscular)
- Age distribution of living patients

The number of patients by disease (including genetic diagnosis) and country are currently not published on the website but can be obtained from the registry team via esid.registry@kenes.com

National registries may publish a similar set of data, e.g. on their websites or in newsletters.

These data can be used in talks and publications without prior consent of the documenting centres or the ESID registry steering committee using the following acknowledgement:

"Data from the ESID online database (www.esid.org)"

2. Patients for a disease-specific study are identified through the ESID database.

Example: an investigator wishes to identify patients with XLA who have developed carcinomas.

Publication: Authorships are negotiated between the investigator and the contributing centres.

In addition, in the methods or in the acknowledgement section, the following statement must be included:

"Patients for this study were (in part) identified through the ESID Online Database."

3. Data from the registry are evaluated, but make a minor point in a larger paper

Example 1: in the context of a review on CVID, an analysis of registry data on the age distribution of CVID patients is performed and included.

Example 2: a study on mechanisms of carcinogenesis in radiosensitive immunodeficiencies uses registry data to document the incidence of tumours in these patients in Fig. 1, but then goes on to address the question experimentally.

Publication: One member of the ESID Registry team, who has extracted the data and/or provided the statistical analysis, is listed among the authors as follows: Name, for the ESID Registry Working Party. As an affiliation note, the following statement is included: ***“The ESID Registry is based on contributions by the following national registries: CEREDIH (France), REDIP (Spain), PID-NET (Germany), UKPIN (UK), IPINET (Italy), AGPI (Austria), the Netherlands, Czech Republic. Additional contributions are received from the following countries: Turkey, Poland, Ireland, Portugal, Belgium, Switzerland, Slovakia, Sweden, Slovenia, Croatia, Serbia, Greece, Belarus, Russia, Hungary, Romania, Ukraine, Estonia, Lithuania, Egypt, Israel.”*** (to be updated accordingly).

For reviews (with restricted authorships), the steering committee can decide that no primary authors are listed and the statement will only be included as an acknowledgement.

4. Data from the registry make up the majority of data presented in the paper

Example 1: a study is proposed for the analysis of all children with CVID documented in the registry.

Example 2: a yearly update of the ESID database project is prepared for publication.

Publication:

- First, second and last authorship for those performing the study.
- Third and further authorships to the contributors to the ESID registry. This includes the members of the ESID registry team involved in data extraction and analysis and representatives from centres contributing patients.
- As many authors as possible (this means as allowed by the journal), one per centre, according to the number of patients included in the study.
- After the last author the statement 'for the ESID Registry Working Party'
- All centres that cannot be listed among the authors, but have participated with patients in the study, should be listed in a footnote or appendix, mentioning the program director and one of the collaborators.
- When a manuscript/abstract draft is finalized, the author e-mails the draft to the ESID registry steering committee (via esid.registry@kenes.com) for review. Further submission of a manuscript is only permitted after approval by the steering committee. Recommendations of the steering committee have to be respected by the authors.

5. Data analysis is restricted to patients from individual centers/national cohort analysis

Procedure: Individual study centres are entitled to analyze registry data from their patients and national registries are entitled to analyze registry data from their nation without the need to involve the ESID registry steering committee in the publication process.

Publication: The following statement must be included in the methods or acknowledgement section:

"The ESID Online Database was used for collecting data for this study."

6. Procedure for studies using the ESID Database for prospective data collection

Example: a study is proposed to collect data on all cases of DOCK8 deficiency via the ESID Database.

Publication: Authorships are negotiated between the investigator and the contributing centres.

In addition, in the methods or in the acknowledgement section, the following statement must be included:

"This study used the ESID Online Database for data acquisition."

7. Studies performed by sponsors of the ESID Database

Example: PPTA has internally analysed data on Ig replacement in CVID patients and now wishes to publish these.

Publication: The sponsor has the right to nominate authors. The members of the ESID Registry team, who have extracted the data and/or provided the statistical analysis, are listed among the authors as follows: Names, for the ESID Registry Working Party. As an affiliation note, the following statement is included: ***"The ESID Registry is based on contributions by the following national registries: CEREDIH (France), REDIP (Spain), PID-NET (Germany), UKPIN (UK), IPINET (Italy), AGPI (Austria), the Netherlands, Czech Republic. Additional contributions are received from the following countries: Turkey, Poland, Ireland, Portugal, Belgium, Switzerland, Slovakia, Sweden, Slovenia, Croatia, Serbia, Greece, Belarus, Russia, Hungary, Romania, Ukraine, Estonia, Lithuania, Egypt, Israel."*** (to be updated accordingly).

When a manuscript/abstract draft is finalized, the author e-mails the draft to the ESID registry steering committee (via esid.registry@kenes.com) for review. Further submission of a manuscript is only permitted after approval by the steering committee. Recommendations of the steering committee have to be respected by the authors.

For further questions regarding the research and publications process, please contact the ESID registry team at:

Email: esid.registry@kenes.com

Phone: +49 761 270 34450

Fax: +49 761 270 9636960

Annex A

Agreement between the European Society for Immunodeficiencies (ESID) and a Documenting Centre regarding the ESID Online Registry

§2

The Documenting Centre shall be and remain the owner of any data it has provided to the ESID Online Database. ESID shall be entitled to make available the “Red Field”-data to the sponsors of the ESID Online Registry for the following purposes: to enable genetic and therapeutic research across different authorised users; for genetic and therapeutic trials; for the treatment and care of patients; for the development and improvement of medication; for evaluations of epidemiologists. The receiving parties of such data ensure to use the data for internal use only, unless they have obtained the prior written consent from ESID to publish them or to use them for publication.

The Documenting Centre retains the right to define the access of other ESID Centres, PID researchers or epidemiologists to its data. These other participating Documenting Centres or researchers shall only have access to the data provided by the Documenting Centre if the enquiring Documenting Centre submits to ESID a respective application in writing, and if the Documenting Centre gives its written consent. Unless otherwise specified, the authorised Documenting Centre shall be entitled to use the data provided by the Documenting Centre to the same extent and for the same purposes as the sponsors of ESID.

ESID shall ensure that the sponsors obtain access to the ESID Online Database only for the purposes as stipulated hereunder and that the access granted to other Documenting Centres corresponds to the written consent given by the Documenting Centre. Moreover, ESID shall obligate all authorised users of the ESID Online Registry not to disclose the data of such database to any unauthorised third party.