

# **PSONET**

**EUROPEAN SURVEILLANCE NETWORK TO MONITOR THE  
LONG TERM EFFECTIVENESS AND SAFETY OF SYSTEMIC  
AGENTS IN THE TREATMENT OF PSORIASIS**

## **The PSONET Code of Conduct**

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## **1. Background**

The PSONET initiative originates from the endeavour to establish a network of independent European population registries, in order to perform coordinated post-marketing surveillance studies aimed at monitoring the effectiveness and safety of systemic agents in the treatment of psoriasis.

The PSONET Code of Conduct originates from the necessity to create an essential document setting out the rules and principles for the PSONET collaboration.

## **2. Scope and Implementation in the Context of “PSONET Collaboration”**

The aim of the Code is to ensure transparency within the PSONET collaboration, setting out rules and principles for good practice registry activity and international collaboration.

**The use of this Code is voluntary but it is a requirement for being part of the PSONET collaboration.**

## **3. Application and Compliance**

Any registry adhering to the PSONET collaboration shall be in compliance with the “CORe requirements”.

### CORe Requirements

- Code of Conduct: Compliance with the rules of the PSONET Code of Conduct.
- Operational Research Standards (ORS): Application of ORS (Annex 1).
- Registry activity: Basic elements of good registry practice for research and evidence (Annex 2).

## **4. General Provisions**

- The primary purpose is to generate data of potential scientific or public health importance and not to promote the sale of a medicinal product;
- The design of research is aimed towards increasing the effectiveness and the safety of systemic treatment for psoriasis;
- The results of the study will be published, preferably in a peer-reviewed journal, or made available for public scrutiny within an acceptable time frame, regardless of the (positive or negative) results and the statistical significance.

## **5. Ensuring Transparency**

A maximum level of transparency on relevant information pertaining to the study is ensured. This includes information on the study protocol and any revisions thereof, and the publication of study findings.

## **6. Study Protocol**

The PSONET protocol is available to anyone within the PSONET collaboration in order to provide general study information on entry criteria and follow-up, set of variables to be merged, pooling of data, statistical analyses, and dissemination of results. The protocols of each individual registries participating in the PSONET collaboration should be made available to PSONET members.

## **7. Data Ownership and Access to Data**

Data originated by national registries belong to the registries producing them and according to rules internal to the individual registries. Relevant data to address specific questions on which an agreement has been reached within the PSONET collaboration should be shared with other registries in an adequate format (individual patient data vs aggregate data), and in a way to make combined analyses possible. This kind of data sharing is a requirement for being part of the PSONET collaboration. By taking into account potential provisions on data ownership and access to data defined in each national registry research contract, aggregate anonymous data could be the only data to share. Data originated by data pooling belong to the PSONET collaboration and should be used only after agreement by all the PSONET members. Any registry within the PSONET collaboration will have access to aggregate data and to the related analyses/results.

## **8. Publication/Reporting of Study Results**

Prior to publication, the Safety Advisory Board will supervise and double check the analyses and the corresponding results.

A clear summary of the main results of the study, whether positive or negative, will be made available to the public.

A full report of all results with a scientific or public health impact will be made publicly available. In case of a (suspected) public health impact, relevant legal provisions will be followed and the respective competent authority(ies) will be informed forthwith and in advance of publication.

The requirements for granting authorship on any article to be published are data provision and/or collaboration to data analyses and/or discussion/interpretation of results.

## **9. Confidentiality**

A maximum level of confidentiality will be sought in relation to any information pertaining to data and results derived from the study until the publication of the study findings.

## **10. Relation with Other Entities**

Any collaboration/relation between the PSONET group and other entities, such as the European Medicines Agency (EMA) or the World Health Organization (WHO), should be agreed on in advance. No specific requirements or restrictions are defined concerning the relation between national registries and the corresponding national regulatory agencies.

## **Annex 1 (Operational Research Standards, ORS)**

### **MAIN CHARACTERISTICS OF THE STUDY:**

- **Research question:** effectiveness and safety of systemic agents, including biologicals (i.e. Tumor Necrosis Factor alpha, TNF-alpha, and T cell targeted molecules), in the treatment of psoriasis.
- **Target population:** all the subjects with active psoriasis who receive, for the first time in their life, at least one single dose of a systemic agent for psoriasis.
- **Primary endpoints:** response to treatment for effectiveness; adverse events and diagnosis of selected diseases for safety.
- **Data source:**
  - exposure: systemic treatment for psoriasis at entry and updates during follow-up;
  - endpoints: for effectiveness, indicators of psoriasis severity, remissions, major disease flare ups, survival within the originally administered therapy, switch to another drug or drug withdrawal because of a lack of response; for safety, selected adverse events and diagnosis of selected diseases during follow-up;
  - covariates: patients' socio-demographic characteristics, anthropometric variables, information on psoriasis and its characterization, previous systemic treatments, selected co-morbidities, pregnancy, hospital admissions, deaths.
- **Standardization and harmonization of core data format and definition within the registries**
- **Data analysis:**
  - descriptive tables;
  - standardized rates;
  - internal and external comparisons;
  - response rates;
  - subgroup analyses;
  - univariate and multivariate analyses;
  - dose-dependent and time-dependent analyses.
- **Quality assurance:**
  - research quality (standardized data);
  - evidence quality (strength of the association, biases, temporal relations, consistency of results with other relevant research).
- **Data review and interpretation:**
  - internal validity (biases, power of the study);
  - external validity (usefulness and generalizability of the study).

## **STRUCTURE OF THE PSONET ORGANIZATION/COLLABORATION**

The main aims of the PSONET collaboration are:

- **sharing of knowledge and experience;**
- **sharing of data in order to perform pooled analyses.**

In order to share registry and personal experience, and theoretical and practical knowledge (as statistical skills), one or two meetings per year are organized. Each registry or country interested in these meetings could participate by contacting Dr. Luigi Naldi, the coordinator of the PSONET collaboration (e-mail: [luigi.naldi@gised.it](mailto:luigi.naldi@gised.it)).

Data sharing in order to perform pooled analyses implies the following steps with the corresponding rules:

- a person or a group interested in a specific question/analysis creates a working group able to address it;
- the working group develops a protocol with definition of the research question, data needed, resources available, time schedule, authorships with the corresponding rules for publication and conflicts of interest;
- each registry interested can participate sharing requested data and following rules set out in the protocol;
- corresponding results will be shared with the other PSONET members and made publicly available through scientific literature.

**AGREEMENT FORM:**

In order to participate in the PSONET collaboration, the following Agreement Form has to be signed.

**Declaration on compliance with the PSONET Code of Conduct for PSONET collaboration**

The lead investigator or a person authorised to sign on behalf of the registry hereby declares for the purpose of collaboration within the PSONET

- to follow the rules and principles of the PSONET Code of Conduct for PSONET collaboration,
- to have submitted the present document to the corresponding individual Advisory Board for approval,
- to inform, without delay, of any change or decision to change that constitutes a deviation from the provisions of this Code.

Name of the lead investigator: \_\_\_\_\_

Date: \_\_\_\_\_

Signature: \_\_\_\_\_



## **Annex 2 (Research and Evidence Quality for Registries – Basic Elements of Good Practice)<sup>1</sup>**

### **RESEARCH QUALITY FOR REGISTRIES - BASIC ELEMENTS OF GOOD PRACTICE**

#### **• Planning**

- Sufficient thought has been given to identifying and capturing all the necessary aspects that are feasible to collect from the outset.
- A written registry plan documents the goals; design; target population; methods for data collection, including patient recruitment; data elements and data sources; a high-level data management plan; plans for protecting human subjects and for data review for quality; and a high-level analysis plan that contains sufficient detail to explain the main focus and proposed methods of analysis.
- The process for identifying serious events is described and a plan is created for reporting, as appropriate and consistent with regulatory requirements.
- A plan for communication of study results is addressed.
- Appropriate personnel and facilities are available, including facilities for secure storage of data.
- A process is established for documenting subsequent modifications to the registry plan.

#### **• Design**

- The literature has been reviewed to guide appropriate data collection.
- The target population is described, including plans to recruit study subjects.
- Specific eligibility, inclusion, and exclusion criteria are specified.
- The size required to detect an effect, should one exist, or achieve a desired level of precision is specified, whether or not the sample size requirement is met.
- The follow-up time required to detect events of interest is specified, whether or not it is feasible to achieve; however, the follow-up time planned is adequate to address the main objective.
- Plans are made for how the analysis will be conducted, including what comparative information, if any, will be used to support study hypotheses or objectives.

#### **• Data elements and data sources**

- Outcomes are clinically meaningful and relevant in that the information is useful to the medical community for decision making.
- Operational definitions of outcomes are clearly defined.
- Important exposures, risk factors, and mitigating (or protective) factors are identified and collected to the extent feasible.

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<sup>1</sup> Glicklich RE, Dreyer NA, eds. Registries for Evaluating Patient Outcomes: A User's Guide. (Prepared by Outcome DEcide Center [Outcome Sciences, Inc. dba Outcome] under Contract No. HHS290200500351 TO1.) AHRQ Publication No. 07-EHC001-1. Rockville, MD: Agency for Healthcare Research and Quality. April 2007.

- The individual(s) responsible for the integrity of the data, computerized and hard copy, are identified; it is determined that they have the training and experience to perform the assigned tasks.
- Data collectors are trained using standard techniques.
- A data and coding dictionary is maintained to provide explicit definitions and describe coding used.
- A quality assurance plan has been created and addresses data editing and verification, as appropriate.
- **Ethics, privacy, and governance**
  - The issues of protection of human subjects - including privacy, informed consent, data security, and study ethics - have been carefully considered and addressed in accordance with local, national, and international regulations.
  - The registry has received review by any required oversight committees (e.g., ethics committee, privacy committee, or institutional review board, as applicable).

## **QUALITY FOR REGISTRIES - BASIC ELEMENTS OF GOOD PRACTICE**

- **Registry participants**
  - Registry participants are similar to the target population, and attention has been paid to minimizing selection bias to the extent feasible.
  - Eligibility (in terms of inclusion and exclusion criteria) is confirmed upon patient enrolment.
  - For safety studies, personnel are appropriately trained to ask about complaints or adverse events in a manner that is clear and specific (e.g., solicited vs. unsolicited) and to know how information should be reported to manufacturers and health authorities.
  - Completeness of information on eligible patients has been evaluated and described.
- **Data elements and data sources**
  - Information has been collected for relevant key exposures, risk factors, and mitigating or protective factors.
  - Patient outcomes are clinically relevant (in terms of information that will assist medical professionals with decision making) and clearly defined. Definitions are provided, especially for complex conditions or outcomes that may not have uniformly established criteria (e.g., specify how an “injection site reaction” is operationally defined).
  - The follow-up period is reasonably sufficient to capture the main outcomes of interest.
- **Data quality assurance**
  - Data are reasonably complete.
  - Reasonable efforts have been expended to assure that appropriate patients have been systematically enrolled and followed in as unbiased a manner as possible.
  - Reasonable efforts have been devoted to minimize losses to follow-up.
  - Data checks are employed using range and consistency checks.

- **Analysis**

- Accepted analytic techniques are used; these may be augmented by new or novel approaches.
- The role and impact of missing data and potential confounding factors have been explored.

- **Reporting**

- A report describes the methods, including target population and selection of study subjects, compliance with applicable regulatory rules and regulations, data collection methods, any transformation of variables and/or construction of composite endpoints, statistical methods used for data analysis, and a description of any circumstances that may have affected the quality or integrity of the data.
- Results are reported for all the main objectives.
- Follow-up time is described so that readers can assess the impact of the observation period on the conclusions drawn.
- The report includes a clear statement of any conclusions drawn from the analysis of the registry's primary and secondary objectives and any implications of study results, as appropriate.
- All authors who are acknowledged have had a meaningful role in the design, conduct, analysis, or interpretation of results.