euresist network

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EuResist Network Partnership Agreement

Between:

EuResist Network GEIE

And

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EuResist Network GEIE is a European Grouping managing the results of research projects carried on by its members and promoting joint activities among them.

In particular, the EuResist Network manages the EuResist Integrated database (EIDB) and the EuResist Prediction Engine.

Members of the EuResist Network GEIE are Informa, Max Planck Institute, Karolinska Institute, University of Siena, University of Koeln, whose representatives compose the Management Board.

1. Partnership

Partnership with EuResist Network is based on scientific collaboration and data sharing for mutual benefit.

Reasons for partnership include either expanding the EIDB with valuable data or contributing to data analysis in scope with the EuResist Network aims or both. Partner's activities and data are protected by the data and authorship policies detailed hereby in the "Contributing to Eu*Resist*" chapter.

Partners will:

- Become members of the EuResist Network Scientific Board in reason of one person per partner institution.
- Provide valuable data for integration in the EIDB *and/or* provide data analysis tool(s) in scope with EuResist Network aims.
- Have access to the EIDB for research proposals following the rules detailed hereby in the "Use of Eu*Resist* data" chapter.
- Be acknowledged in papers and communications making use of EIDB data as detailed hereby in the "Authorship rules" chapter.
- Be involved in scientific and dissemination activities promoted by the EuResist Network.

- Be acknowledged on the EuResist Network website.

*2. The Eu*Resist *Network Scientific Board*

The Eu*Resist* Network Scientific Board is composed by the Management Board of EuResist Network (Francesca Incardona, Thomas Lengauer, Rolf Kaiser, Anders Sonnerborg, Maurizio Zazzi) and by all the partners of the Eu*Resist* Network (in reason of one person per partner institution).

Objectives and functions

1. To suggest research proposal based on the use of the data stored in the EIDB.
2. To evaluate the scientific adequacy of research proposals, made by third parties, that require the access to the data stored in the EIDB. Each proposal that requires the use of the Data stored in the EIDB, coming from either a member of the Scientific Board and/or third parties, must be approved by the Scientific Board.
3. Decisions on approval or rejection of research proposals based on the EIDB are taken by simple majority.
4. The Scientific Board can be interrogated and answered by email but anyway on the basis of a written document.
5. It is duty of the Scientific Board to provide approval or rejection of proposals within 15 days from receipt.

3. Contributing to EuResist

3.1 Data integration

The task of integrating new data from partners into the EIDB will be carried out by the Eu*Resist* Network team with the collaboration of the data provider, limited to providing information on database platform and schema and sending data via the method agreed upon.

Integrating data ensures a quality control made by the EIDB administrator at the advantage of the contributing centre. Partners will receive quality control feedbacks from EuResist.

3.2 Data protection

Data provided by a partner always remain the property of the partner.

Data are contributed by the partner solely for the development of the treatment response models that are the focus of the Eu*Resist* Network. Any other use is subject to information to and explicit approval by the partner

The partner reserves the right to have its data permanently removed from the EIDB at any moment without any need to justify this decision. Should this occur, the data are considered available only for pending papers and/or presentations already agreed upon, i.e. submitted for publication.

Should the Eu*Resist* Network GEIE end, each external dataset will be removed from the EIDB unless the partner explicitly requests that the data remain in the EIDB.

3.3 Description of data needed

The primary aim of EuResist is to provide an accurate estimate of the probability of success for any antiretroviral treatment based on a set of input information. Thus, the system must learn from quality assured patient cases. The minimum data required for such machine learning step include HIV sequence(s) coupled with the treatment(s) administered and a viral load measurement at 8-week and possibly later (e. g. 24-week or 48-week) follow-up.

A more complete input dataset has been shown to provide significantly more valuable statistical learning. The EuResist prediction engine does indeed generate more accurate estimates of the probability of success when the complete baseline information is available. Additional data with respect to the minimal feature set described above include baseline viral load and CD4 counts, indicators of past antiretroviral drug exposure (number of previous treatment lines and binary descriptors of the use of individual drugs) and basic patient demographics (gender, age, route of infection).

More exhaustive dataset including a variety of different parameters like side effects, co-infections, information on adherence etc. are clearly welcome. Indeed, although these parameters have not yet been considered for training the prediction model, their use in the future is envisioned to improve the system.

In summary, depending on the nature of the data provided there can be different levels of contribution to further developing the EuResist engine. In general, the most productive approach is to upload all the available data and then extract what required for statistical learning.

The following table summarizes the type of information and levels useful for the EuResist engine.

Minimal dataset required	Baseline HIV sequence (all the genome regions coding for drug targets are considered)
	Treatment administered
	Follow-up viral load
Complete dataset considered in EuResist version 2 (additional with respect to the minimal dataset)	Baseline viral load
	Baseline CD4 counts
	Patient demographics (gender, age, route of infection)
	Number of past treatment lines
	Binary indicators of previous use of individual drugs
Additional information considered for future versions	HBV and HCV coinfections
	Drug side effects
	Adherence levels

4. Use of EuResist Integrated DataBase by third parties

4.1 Agreement on data contribution

The EIDB is open for research proposals coming from third parties. Requests must be submitted to the Eu*Resist* Scientific Board and will be evaluated on the basis of scientific quality, compliance

with ethical rules (submission to ethics committees may be required) and potential complementarity or overlap with ongoing scientific work carried on by the Eu*Resist* Network team.

Notwithstanding the Scientific Board decision, any partner can decide for itself to deny access to its own data for any reason.

4.2 Data integration

The task of integrating the Eu*Resist* Integrated DataBase (EIDB) with other data sets will be carried out by the third party data collector with the collaboration of the Eu*Resist* team, limited to providing information on database platform and schema and sending data via the method agreed upon.

4.3 Data protection

Data provided by the Eu*Resist* Network to any other third party centre remain the property of Eu*Resist* (that is to say of its contributing partners according to its foundation rules).

Data are contributed solely for the scientific objective(s) specified in the request to the Eu*Resist* Network Scientific Board; any other use is subject to information to and explicit approval by the Eu*Resist* Network Scientific Board. Proposed studies will be carried out only on the subset of data belonging to the contributing centres who gave their approval.

The Eu*Resist* Network and each of its partners reserve the right to have their data permanently removed from the external data set at any moment without any need to justify this decision. Should this occur, the data are considered available only for pending papers and/or presentations already agreed upon, i.e. submitted for publication.

Should the Eu*Resist* Network end, its EIDB will be removed from the external data set. However, any specific partner reserves the right to requests that his or her data remain in the external data set.

4.4 Authorship policy

Authorship of publications using the EIDB data is regulated as follows:

1. All individuals making a major contribution to a publication are acknowledged by the inclusion of the individual's name as an author. Major contribution is defined in agreement with the rules of the International Committee of Medical Journal Editors (ICMJE; website http://www.icmje.org/index.html#authorship).
2. The name of the individual who conceived the study and drafted the manuscript/abstract is listed as first author, with subsequent names listed in order of decreasing contribution.
3. Alternatively, an individual who makes a major contribution to a publication may opt to be listed as last author to identify the research group or unit in which the work was done even though that individual's overall contribution is not less than those of individuals listed earlier on the by-line.
4. Data provider partners designate their representatives to be included as authors.
5. The number of names listed on the by-line as representatives of the data provider partners is obtained as the maximum number of authors allowed by the journal/congress minus the

number of authors who contributed substantially to study conception and design, data analysis and interpretation, manuscript preparation and approval.

6. The priority list of data provider partners' representatives to be included as authors reflects the proportion of cases in the study contributed by each data provider.
7. Data provider partners' representatives not included as authors because the maximum number of names has been reached are considered for authorship of future papers based on the overall cumulative contribution provided to papers where they were not included in authorship.
8. The Eu*Resist* Network should be listed as author by adding "the EuResist Network Study Group" after the last author on the by-line. Or, the EuResist Network should be acknowledged in the acknowledgement section by saying "This study benefited from data provided by EuResist Network EIDB"
9. All other contributors are listed in an acknowledgments section.

5. Ethics

All the patient information contained in the EIDB and its future updates and upgrades is anonymised. Patients whose data have been included in the EIDB via the original data sources have signed an informed consent indicating their permission to use their own data for non-commercial purposes. EuResist itself does not deal with ethical permissions. Data providers have the responsibility to grant that local and national ethical committees have approved the individual databases for anonymised research purposes.

EuResist does not involve either storage or any work on biological samples. EuResist primary goal and additional research activities are limited to data handling and elaboration in agreement with the specific studies approved by the Scientific Board. Should any participant to any research proposal require ethical approval for the specific proposal it is understood that the individual participant would take care of this step locally.

IN WITNESS WHEREOF,

the parties hereto have duly executed this Agreement as of […date] by their authorized representatives.

EURESIST NETWORK GEIE

By

Printed Name: Francesca Incardona

Title: Administrator

NAME, INSTITUTION OF THIRD PARTY

By: _____

Printed Name:

Title: