RD-Connect GPAP Data Access Committee
Terms of Reference

Preamble

1. This committee is hereby established to act as the RD-Connect Genome-Phenome Analysis Platform (RDC-GPAP) Data Access Committee, hereinafter referred as the DAC.
2. The following constitutes the Terms of Reference of the RDC-GPAP Data Access Committee.

Purpose

1. The DAC is formed with four main purposes:
    a. To review and grant access for all user accounts requests to the RDC-GPAP, and to rule on circumstances where a user's access may be revoked for lack of adherence to the Code of Conduct or other breach of best practice.
    b. To review all requests from users pertaining to Commercial/Pre-commercial activities to access RDC-GPAP; to evaluate their proposed projects and to perform a yearly follow-up to ascertain its correct development.
    c. To review all requests for exceptions to the default embargo periods, in line with RDC-GPAP standard procedures for embargo and availability of data.
    d. To review requests for access to data outside the access provided through the RDC-GPAP interface, including access to raw data submitted to the European Genome-Phenome Archive (EGA), and access to aggregated data that may be requested for specific research purposes.
2. In pursuing its remit, the DAC provides advice and professional guidance to the owner of the RDC-GPAP, the Consorcio para la Explotación del Centro Nacional de Análisis Genómico (Consorcio CNAG), with whom ultimate liability rests. They DAC members shall not be liable for any mistake of judgment or any other action made, taken or omitted by them in good faith. The advice of the DAC aims to ensure access to data in RDC-GPAP is controlled according to best practices for security of sensitive data, while nevertheless ensuring that data sharing for the benefit of rare disease research and for patient benefit is encouraged.
3. Amendments of these terms of reference may be made at any time with the agreement of the DAC and the Consorcio CNAG.

Chair and core members of the DAC

1. The Chair of the DAC will be elected/re-elected biennially by the panel members.
2. The DAC will have no less than three and no more than five members at any time. There should be one representative of a patient organisation in the field of rare diseases and one of the hosting institution (Consorcio CNAG) at all times.
3. Other individuals or representatives of groups or organisations that may have an interest in the RDC-GPAP may be invited to join the DAC at any time with the agreement of the DAC itself and the Consorcio CNAG.
4. The members of the DAC provide their services voluntarily and can withdraw at any time by providing confirmation to the Chair.
5. All DAC members will be asked to complete a declaration of all potential conflicts of interest, which will be a public document available to anyone on request. In cases where a potential conflict may arise with regard to a specific user request (e.g. due to existing collaborations with that user), the DAC member should disclose this to the other members for transparency. Such knowledge does not automatically disqualify the member from

participating in discussions about the potential new user and the member is not automatically obliged to recuse themselves. The member and the DAC should act at its own discretion in each case to decide whether the relationship constitutes a substantive conflict of interest.

6. Consorcio CNAG has overall oversight of the DAC and can intervene to remove or add members.

Standard Operating Procedures

General principles

1. The DAC will convene via e-mail using a dedicated mailing list, and may additionally convene by teleconference for cases where any DAC member feels additional discussion is necessary.
2. The DAC will vote on all requests via e-mail within 10 working days.
3. A minimum of two thirds of the DAC must participate for a vote to be valid and two thirds of the full DAC (not just those participating) must vote in favour for a decision to be accepted.

Validating new users of the RDC-GPAP

The DAC plays its role in RDC-GPAP user validation as follows:

1. Access to RDC-GPAP is granted at a research group level. Requests to create a new RDC-GPAP group are received by the RDC-GPAP Helpdesk through the "User Registration" online submission form. Only researchers complying with the following criteria can request the creation of a new RDC-GPAP group:
   1.1. To be a Principal Investigator / Group Leader.
   1.2. To carry out scientific research in rare diseases.
   1.3. To be willing to submit / access data in RDC-GPAP.

   In addition, the "User Registration" form requires the following information:

   1.4. The reason for requesting access to RDC-GPAP.
   1.5. The name of the research center, group website and institutional email.
   1.6. A copy of the Adherence Agreement signed by the PI / Group Leader and the legal representative of the institution where the PI is working. Both signatures should be either valid eSignatures issued by a Certification Authority or handwritten signatures. In case of handwritten signatures, a copy of an ID document must be provided by both the PI and the legal representative.
   1.7. Relevant scientific publications.
   1.8. Names and emails of users to be added to the newly formed RDC-GPAP group.

   The RDC-GPAP Helpdesk reviews the registration request for completeness and validity against the predefined criteria and creates a checklist for review by the DAC.
2. The DAC receives from the RDC-GPAP Helpdesk details of the new user registration requests, and decides on their approval.
3. Approvals of new users for large multi-partner projects may be received as a single "batch" of requests that have been pre-validated by the coordinators of the project in question.

Reviewing requests for embargo extensions

In accordance with the Data Access Policy, submitters may request that their data remains private to their own

group for a specific period after submission to enable them to analyse their own data before it becomes visible to other users. These requests are made via the online submission form at the time of data submission and have specific approval requirements as outlined below.

The DAC plays its role in embargo extensions as follows:

1. Embargo periods of 0 to 6 months are automatically approved by the system. They are individually logged and may be provided to the DAC on request, but no specific approval on the part of the DAC is required.
2. Embargo periods of >6 months may be requested by sending an email to help@rd-connect.eu at the time of submission with a specific justification. In these cases, the RDC-GPAP Helpdesk collates the information on the submission and the specific justification and forwards it to the DAC. The DAC rules on each request within its standard timeframes.
3. In certain cases, large-scale submitting projects may request specific exceptions to the standard Data Access Policy, for example project-wide embargo extensions. It is the role of the DAC to rule on such requests in line with good scientific practice, weighing up the requirements for rapid data release against the justification for extension and the overall concept that submission to RDC-GPAP is to be encouraged as it does contribute to broader data sharing in the longer term.
4. In line with the Code of Conduct for RDC-GPAP Users, requests for embargo extension must be made at the time of data submission. Retrospective requests are not accepted.

Approving requests for access to data outside the RDC-GPAP

Most data access takes place entirely within the RDC-GPAP system, where users can analyse their own data and access data from other submitters. However, in certain cases there may be requests for access to data that fall outside the access a user obtains through an RDC-GPAP account. The DAC plays the following role in these cases:

1. For each dataset existing in RDC-GPAP, the corresponding raw data is stored in the EGA for archival purposes. The EGA requires a Data Access Committee to govern access to each dataset it stores. On submission to RDC-GPAP, users must specify whether their submitted data falls under a specific Data Access Committee of their own choosing (for example a project-specific DAC, e.g. NeurOmics DAC or Solve-RD DAC) or whether it accepts the RDC-GPAP DAC. The Committee acts as the DAC for datasets in which the submitter selected RDC-GPAP.
2. Access to datasets held by the EGA is requested through the standard EGA system, which requires that the user already has an EGA account and has gone through the standard EGA validation processes. The access request will be sent to the DAC mailing list.
3. The DAC will rule on the access request within its standard timescales in line with the following principles:
    3.1. Requests from users who are already RDC-GPAP users should normally be approved as a matter of course, as the user already has access to the data in question within the RDC-GPAP.
    3.2. Requests from new users should be evaluated based on the justification provided in the EGA access request. Where it appears a user, who has requested access via EGA, may benefit from RDC-GPAP access, the DAC in its function as EGA DAC may also recommend this to the user, either in addition to acceptance of the request for the raw data or as an alternative. Users who wish to request RDC-GPAP access would then apply via the standard RDC-GPAP procedure.
    3.3. In certain cases, researchers outside RDC-GPAP may wish to obtain aggregate data on the patients, variants or phenotypes held within the RDC-GPAP. This may also apply to commercial entities who are not entitled to become full users of the RDC-GPAP. Such requests will never result in the disclosure of

individual-level data, which can only be obtained with an RDC-GPAP account or by access to the raw data at EGA through a valid EGA account and permission from the DAC as above. Aggregate requests will be referred to the DAC, who will rule on the access request within its standard timescales. Since creation of the aggregate dataset requires time and effort on the part of the RDC-GPAP staff, this should be considered in the ruling, in addition to consideration of the reasoning and benefits behind the request itself.