Code of practice for integrated user access to RD-Connect platform for health-related information and human biological samples[1]

Effective as of 9 November 2015.

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1. Definition of terms

Personal data

Any information relating to an identified or identifiable natural person ('data subject'). (As defined in Directive95/46/EC, article 2a) Personal data may be available as recorded and registered data or in the format of human biological samples under the provision that there is a code through which the sample can be connected to the identity of an individual donor.

Human biological samples

Constituent parts of the human body, or human biological material, including organs and parts of organs, cells and tissues, and body fluids.

Identifiable person

One who can be identified, directly or indirectly, in particular by reference to an identification number or to one or more factors specific to his physical, physiological, mental, economic, cultural or social identity.
(As defined in Directive95/46/EC, article 2a)

Processing of personal data

Any operation or set of operations which is performed upon personal data, whether or not by automatic means, such as collection, recording, organization, storage, adaptation or alteration, retrieval, consultation, use, disclosure by transmission, dissemination or otherwise making available, alignment or combination, blocking, erasure or destruction.
(As defined in Directive95/46/EC, article 2b)

Data controller

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[1] This code of practice is adapted from a draft version by EHR4CR, 27 August 2014. It was being revised in Barcelona 27th of January 2015, at the Annual Meeting of RD-Connect, acknowledging comments from: Bartha Knoppers. Olaf Riess, Manuel Posada, Peter-Bram't Hoen, Mirella Filocamo, Marina Moa, Sabina Gainotti, Pauline McCormack and Mathieu Boudes of EURORDIS on previous drafts. It was approved at the Executive Management Committee of RD-Connect 2015-06-11 It was approved by Parc de Salut MAR - Clinical Research Ethics Committee in Barcelona 2015-10-29

It should always be referred to according to the announced date. It may need revisions dute to changes in the regulatory frameworks.

The natural or legal person, public authority, agency or any other body which alone or jointly with others determines the purposes and means of the processing of personal data; where the purposes and means of processing are determined by national or European Union laws or regulations, the controller or the specific criteria for his nomination may be designated by national or European Union law.
(As defined in Directive95/46/EC, article 2d). Within RD-Connect the submitter of data is the data controller.

Data processor

The natural or legal person or any other body which processes personal data on behalf of the controller. Within RD-Connect the *centre nacional d'anàlisi genòmica (cnag)* in Barcelona is data processor on behalf of RD-Connect.

Secondary use of data

Processing of already existing health-related personal information for a purpose different from the purpose for which it was originally collected.

Identification, coding and anonymised data

(As defined by the European Medicines Agency 2002, adopted by The International Conference on Harmonisation of Technical Requirements in 2007 and endorsed by the European Union, Committee for Human Medical Products in 2008. Adapted here to fit both personal data and identifiable biospecimens)

Identified data

Data labelled or linked to the individual in a way that makes them directly identifiable (name and surname or social security numbers). There is no identified data within the RD-Connect platform.

Coded data (may be single or double coded)

Personally identifying information is removed from data and bio-specimens and replaced with a code. In the case of double-coding, two or more codes are assigned to the same donor's data held in different data sets, with the key connecting the codes back to the donor's direct identifiers held by a third party and not available to the researchers. The RD-Connect platform contains coded data.

Anonymised data

Data and samples that have been identified earlier or coded, but the identification, or the code and the code key have been destroyed, and thus there is no longer any link to the individual.

Anonymous data

There are no links to the individual donor, the data and bio-specimens were never associated with identifiers, and the risk of identification of individuals is very low. There may be general descriptions such as 'man, aged 50–55

years, cholesterol level 240 mg per 100 ml.'

Unique identifier

A unique identifier for research purposes is a random sequence of characters that is unique to each research participant, regardless of the study, without exposing personally identifiable information. The basic rationale of a unique identifying system is that a medical researcher puts identifying information about a research participant into a client application that in turn sends encrypted information to a server application, which then returns a generated unique identifier for that individual. Once this operation has been finished the encrypted data used for generating the unique identifier is deleted at the server and only the unique identifier is preserved. The data controller will create a unique identifier before the data is transferred to the RD-Connect platform.

Aggregated data

Data of several individuals that have been combined to show general trends or values without allowing identification of individuals.

Incidental finding

A finding concerning an individual research participant that has a potential health or reproductive importance and is discovered in the course of conducting research or diagnostic procedures but is beyond the aims of the study[2].

Genetic data

All personal data relating to the genetic characteristics of an individual, inherited or acquired, as a result of an analysis of a biological sample from the individual in question, in particular by chromosomal, DNA or RNA analysis or analysis of any other element enabling equivalent information to be obtained.

Broad consent

Consent for an unspecified range of future research projects subject to a few content and/or process restrictions, e.g. ongoing governance.

Withdrawal of consent

A research subject has the right to withdraw consent at any time without justification. In case research subjects withdraw their consent for use of their data, the data will be maintained up to the point of withdrawal. The data controller is responsible for deleting all data to be withdrawn, unless an applicable law would prevent it.

2. Aim

The aims of this Code of Practice are: to enable the process of clinical development in rare diseases through research; to ensure collaborative research towards innovation, quality, safety and value in health care; and to protect the privacy of patients and research subjects.

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[2] As defined in Wolf SM, Lawrenz FP, Nelson CA et al: Managing incidental findings in human subjects research: analysis and recommendations. J Law Med Ethics 2008; 36: 219–248, 211.)

3. Legal and ethical framework

All proceedings in accordance with this Code of Practice should be compliant with national and European law. It is the national law of the data controller/person responsible for a registry or collection of personal data that applies to the processing of data, irrespective of where the data is used. Processing must be compliant with the provisions of the informed consent and/or decision of an Ethical Review Board, or else compliant with national law.

The aim of promoting clinical development through research while protecting privacy of patients and research subjects is motivated by The Charter of Fundamental Rights of the European Union (2010/C 83/02). This charter emphasizes the right of each individual to integrity within the fields of medicine and biology, implying a free and informed consent according to the procedures laid down by law (Article 3). Article 8 of the Charter grants the individual the right to the protection of personal data implying that the processing of such data requires consent of the person concerned or other legally-recognized means. These articles conform with the European Convention for the Protection of Human Rights and Fundamental Freedoms, the Social Charters adopted by the European Union and by the Council of Europe.

These rights may be motivated by a fundamental respect of each individual's autonomy and right to have control of matters related to oneself, e.g. the processing of personal data. They may imply a right to know about genetic and other medical information about oneself but also, as has been frequently discussed in the ethical and legal literature, the right not to know such information. In addition to these autonomy rights the Charter of Fundamental Rights of the European Union also lays down rights of each individual to social security benefits and social services in cases of illness (Article 34) and the rights of access to preventive health care and the right to benefit from medical treatment under the conditions established by national laws and practices (Article 35). As described, the charter of the European Union recognizes both the privacy right leading to requirements of respecting autonomy, obtaining consent etc., and the right to health care and social services in cases of illness as fundamental individual rights, notwithstanding that there may also be societal and public health related interests concerned.

In order to balance these fundamental rights there are several information and consent procedures available to be used in different contexts. Broad consent for the use of coded or anonymised and aggregated data is the preferred solution in prospective sampling and collection of data. Renewed consent for secondary purposes using previously collected samples and data where broad consent has not been used is recommended as long as this is practically feasible and does not jeopardize the right of patients and research subjects to

benefit from medical research. In such cases the basis for processing of personal data should be replaced with a decision by an Ethical Review Board.

Sharing data and biological samples (bio-resources) is essential for accelerating biomedical research projects that provides benefits to current and future patients. Research conducted through biobanks and registries is more effective if access to sufficient and quality data and biological samples is granted. The use of data and samples is maximized through data sharing. Ensuring secure data and sample sharing ethically and legally protects bio-resources, as well as the wishes of the donors to contribute to research.

The following five principles for the stewardship of bio-specimens and data repositories constitute the common premise for sharing and access and apply to all users of the RD-Connect platform.[3]

I. Respect for privacy and autonomy: stewardship implies protection of participants' privacy. Privacy protection measures should be in place and informed consent must provide provisions for future as yet unspecified research using data and bio-specimens.
II. Reciprocity: stewardship also implies giving back. Feedback of general results should be channelled to institutions and patients.
III. Freedom of scientific enquiry: stewardship should encourage openness of scientific enquiry, and maximize data and bio-specimen use and sharing so as to exploit their full potential to promote health.
IV. Attribution: the intellectual investment of investigators involved in the creation of data registries and bio-repositories is often substantial, and should be acknowledged by mutual agreement.
V. Respect for intellectual property: the sharing of data and bio- specimens needs to protect proprietary information and address the requirements of institutions and third-party funders.

Article 1 – General provisions

The principles of protection do not apply to data that have been rendered anonymous. In accordance with Recital (26) of Directive 95/46/EC, to determine whether a person is identifiable, account should be taken of all the means likely reasonably to be used either by

[3] See: Mascalzoni D, Dove E, Rubinstein Y, Dawkins H, Kole A, Mc McCormack P, Woods S, Riess O, Schaefer F, Lochmüller H, Knoppers B, Hansson M, International Charter of Principles for Sharing Bio-specimens and Data, European Journal of Human Genetics, Online: DOI EJHG.2014.197 and see also the Global Alliance for Genomics and Health, *Framework for Responsible Sharing of Genomic and Health-Related Data* (www.genomicsandhealth.org)

the controller or by any other person to identify the said person. This Code aims at addressing the processing of data to be used or re-used in collaborative research projects.

This Code is inter alia compliant with:

- Art. 8 of the European Convention on Human Rights
- Convention for the Protection of Individuals with Regard to Automatic Processing of Personal Data 1981 (convention 108)
- Charter of Fundamental Rights of the European Union (2010/C 83/02)
- Directive 95/46/EC of 24 October 1995 on the protection of individuals with regard to the processing of personal data and on the free movement of such data

Article 2 – Collection, use and transfer of data and samples

RULE 1: The entity providing personal data to the collaborative project shall verify that:

- The initial collection of these data has been compliant with the requirements of the original purpose.
- The collection and the provision of the data to the collaborative research projects meets all legal requirements to which the entity is subject.
- Further storage and processing of the data after completion of a collaborative research project is in compliance with applicable law.

RULE 2: The entity which provides personal data to a collaborative project shall document any restriction of use or obligation applicable to these data (e.g., the limited scope of purpose imposed by the consent form, the obligation to report incidental findings, etc.).

RULE 3: The secondary use of data in collaborative research projects shall take place using anonymised data. If however the purposes of the research cannot be achieved using anonymised data, coded data may be used pursuant to this Code. The project shall decide, based on the scientific purpose, legal constraints, and the benefits or risks of harm to research subjects, whether anonymised or coded data shall be used.

RULE 4:

In compliance with this Code data can be shared within the scope of the project independently of geographic boundaries.

RULE 5: Coded data is considered personal data (in accordance with Directive 95/46/EC)

Article 3 – Protection of anonymised data

RULE 6: Aggregated data is considered as anonymised data.

RULE 7: Anonymised data should receive adequate protection against future risks of re-identification.

Article 4 – Information, consent and withdrawal

1. Basic information and consent for prospective research projects

RULE 8: Information and consent procedures shall be approved by the relevant ethics board

RULE 9: Data collectors collecting personal data for a prospective collaborative research project shall inform the study participants about the project in an appropriate manner, including

- the identity of the data controller
- the voluntariness of the collection of data/samples
- the broad/general purposes of the processing
  the nature of the processed data, including its type (identifiable, coded, anonymised)
- the existence of the right of access to, and the right to rectify the data concerning them
- if the research project reasonably anticipates the sharing of data across research groups and national borders
- if complementary information will be added through linkage to different data registries, medical records, etc.
- if the project involves genetic and other molecular analyses
- if the project involves collaboration with both academic and commercial partners
- foreseen secondary use of study participants' data (anonymised or coded) in future research projects
- if information about project results and incidental findings will be provided and the process for this if applicable, and
- that consent may be withdrawn and how this is done

2. Information and consent procedures for previously collected samples and data

RULE 10: For the use of previously collected data and bio-specimens where consent is absent or not fit for purpose, an assessment has to be made by an ethics board governed by applicable national law. Re-consent, notification, opt-out and implied consent or absence thereof are all available and legitimate depending on national legislation and should be selected after a proper balancing of autonomy rights, benefits, risks of harm and right to medical care as described in the legal and

ethical framework of this Code of Practice.

3. Information on project results and incidental findings

RULE 11: Research project results or outcomes should be made available to study participants in a manner allowing non-specialists to understand the results.
RULE 12: If data are still identifiable, incidental finding should be communicated to the initial collector of the data in accordance with what has been described in the information and consent form.

4. Consent withdrawal

RULE 13: Study participants have the right to withdraw their consent at any time without justification.
RULE 14: In case study participants withdraw their consent for use of their data, data but not already derived data or results shall be erased from all research project databases (if still identifiable and unless applicable law requires further storage or use). All data used in the RD-Connect platform are derived results.

Article 5 Sharing and access to data and samples

RULE 15: Material Transfer Agreements should always be used to govern material transfer between parties. Data Transfer Agreements should be used with parties outside EU and where there is no Safe Harbour clause, or with countries accepted by the European Commission in accordance with Article 25, Directive 95/46/EC. Using standard EC contract clauses, e.g. Commission Decision 2001/497/EC, C(2004)5721.[4]
RULE 16: Data and bio-specimens shall always be collected, stored and exchanged in a secure manner, through secure channels.
RULE 17: Access to and use of data and samples should always be based on the scientific validity, quality and potential success of the request to use of data. Those who contribute, collect, curate and annotate samples/ data are entitled to a maximum of six months from

[4] Having regard to a recent decision in the Court of Justice of the European Union (C-362/14, Schrems), where the Commission decision on Safe Harbor for transfer of data to the USA was invalidated, it is suggested in this Code of Practice, in expectancy of further clarifications of the implications of this ruling for research, that in all collaborations with partners in the USA, the partners enter into a Data Transfer Agreements ensuring an adequate level of protection in relation to European data protection principles

submission for exclusive use of the data. When applicable consortia of researchers may have an extended embargo, e.g. within Neuromics this period is maximum 12 months, making data openly available 18 months from submission.

RULE 18: The RD-Connect Platform will provide transparent procedures for authorisation of access to the platform and for the running of the services of the platform. In case RD-Connect will no longer be funded storage of data will be arranged with long-term funded European infrastructures.

RULE 19: The authority of the requestors should be demonstrated through an adherence agreement following this Code of Practice. Proper attribution and intellectual property should be accorded as appropriate, and the security of the data and samples should always be ensured.

RULE 20: Sharing of data and bio-specimens shall follow criteria for the acknowledgement of intellectual contributions and originality through rules of authorship and intellectual property rights.

RULE 21: Quality of data and bio-specimens shall be ensured by the provider.