Beyond One Million Genomes

1+MG Transparency and Consent Recommendations

Recommendations for the content of 1+MG information sheets and consent forms

v2.0 June 2023
[Changes in June 2023: introductory section 1.1]

B1MG PROJECT, WP2, Task 2.2 & Task 2.4.

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1. Introduction

1.1. Purpose

The transparency and consent guidance is a document that should help to compile GDPR and ethical compliant information necessary to provide if data are intended for secondary use. The document also includes a consent guidance where consent can be an informed consent under ethics regime and/or also consent as a legal basis under the GDPR. The guidance is therefore largely applicable independent of the chosen legal basis. Where consent as a legal basis is a relevant element, this is pointed out in the text.

This document can serve as a general guidance for transparency and consent in secondary use also beyond the 1+MG initiative. It describes what elements have to be covered. The content of a concrete information and consent sheet can only be compiled if the data governance for the secondary use is agreed.

1.2. Background

The 1+MG initiative aims to promote responsible cross-border access and secondary use of genomic and related-health data across Europe for research, healthcare, and policy-making purposes. This document provides consent recommendations for prospective data collections intending on making data available cross-border through a repository for research (where the exact projects cannot be fully identified at the time of recruitment).[1] The guidance focuses primarily on information and consent *content* elements, as consent models and processes[2] may vary across countries and contexts. Information content is also important for the transparency requirements under the GDPR, which have changed from the requirements under the Data Protection Directive 95/46/EC and where not all information sheets have been adapted to these changes. These content elements can also be used to design information for re-consenting or notifying individuals that their data will be included in such a resource.[3]

1.3. Nature of the Recommendations

Recommendations are made that 1+MG adopt 1) minimum requirements (MUST); 2) best practices (SHOULD); and 3) points-to-consider (non-directive). If a minimum requirement is missing, this may mean that a Data Holder cannot legally or ethically make data available through 1+MG, or can only do so subject to special data and access and use conditions. Best practices may also constitute national legal requirements in some countries.

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[1] Secondary use for healthcare and policy-making will be addressed separately. The use case for policy-making purposes must be more fully developed before relevant consent guidance can be provided.

[2] This document focuses on consenting adult populations. Additional considerations for minors and other vulnerable populations are addressed in the 1+MG Special Subjects Policy.

[3] A future checklist will be developed outlining minimal requirements when assessing existing consents to determine if legacy data collections can be used for research and accessed cross-border. Making legacy data collections available will be greatly facilitated by the proposed European Health Data Space legislation. However, where data are made available through a separate data resource like the 1+MG, it will still be required that dedicated information is provided and an own legal basis for the data transfers to and from the resource is established.

The recommendations are informed by the legal requirements of the European *General Data Protection Regulation* (GDPR)[4], the interpretive guidance of the European Data Protection Board (EDPB), research ethics principles[5] and guidelines, as well as ethical and legal data governance principles, such as those outlined in the draft *Data Governance Act*, and implemented in the 1+MG Data Governance Policy. Ethical requirements are in particular based on the *International Ethical Guidelines for Health-related Research Involving Humans* by CIOMS. Justifications and explanations are provided. Legal consent requirements depend on the legal basis selected under the GDPR Art. 6 and Art. 9. The guidance provided is largely independent of the legal basis, with *caveats* provided where a consent legal basis under the GDPR may have a stricter regime with respect to information related to consent, scope of the consent, interpretation of what counts as "freely given" as well as in consequences of withdrawal.[6] Requirements for consent as a legal basis may also depend on national laws.[7] Some illustrative examples are provided. National advisory bodies (e.g., ethics committees) are expected to provide additional, nationally-tailored guidance. It is the ultimate responsibility of the organisations involved in collecting data to identify and comply with all norms applicable to their activities.

This guidance is agnostic to different collection and sequencing contexts across Europe[8], including: population databases, genomic research projects, precision medicine clinical trials, genomic medicine initiatives, as well as clinical care (such as predictive, diagnostic or confirmatory genome sequencing). The guidance is designed for any organisation who plans to make data collected in a primary context available through a repository for research projects, where the details of these projects cannot be fully identified at the time of the data collection (or even at the time of the transfer to the repository). Some practical implementation examples are provided to facilitate application of the guidelines in specific contexts.

As 1+MG has not yet determined all aspects of its organisation structure, data governance and legal framework, some key information elements have not yet been fully defined. These elements are relevant to provide transparency and to obtain a valid informed consent.[9] 1+MG is working to clarify these elements so that concrete wording or even a 1+MG specific part of the information sheet, where applicable, can be provided as an appendix in future versions of these guidelines.

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[4] Whole genome sequence data and related-health data included in 1+MG will generally be treated as pseudonymised data (which is personal data).

[5] Including respect for persons, beneficence, and justice with a focus on the main ethical concerns raised by the informed consent process in the context of genomics.

[6] E.g., depending on national law or authoritative interpretations, this may include greater specificity of purposes and recipients; more details about the scope of data subject rights (especially if data are accessed by downstream controllers); and potential power imbalances between controllers (public bodies) and data subjects precluding consent.

[7] E.g., National, regional or sectoral data protection law, medical research law, health law, bioethics law, biobanking law, health research regulations.

[8] The territorial scope is primarily focused on national, regional or institutional data collections established in Member States of the European Economic Area (EEA) who are signatories to the 1+MG Initiative. It is possible that other countries outside the EEA (e.g., UK, Switzerland) are also permitted to contribute collections. Data access may be provided to researchers across the EEA and globally, under appropriate conditions.

[9] The 1+MG as recipient, the defined purposes for which data are made available and the decision making processes need to be defined for obtaining an informed consent, not just under the GDPR but also under ethics principles. See CIOMS 2016 (12); WMA 2016 (12).

1.4. Background

The collection/generation of genomic and related-health data and widespread use for research and healthcare raises a number of ethical issues around informed consent. This includes the risk of privacy breaches; psychological distress due to the type and amount of personal data being processed and shared; risks of harm if data are misused or misinterpreted; the handling of results and incidental findings that have implications for the health of participants and/or their families, including limitations of health care systems to provide adequate follow-up care; and issues of vulnerability (e.g., to discrimination) related to factors including cultural, linguistic, and socio-economic considerations.[10] Ethical issues in genetic/genomic research include the risk of therapeutic misconception; the risk of misunderstanding the purpose and design of this type of research as compared to clinical trials testing medical interventions; and misunderstanding of the risk–benefit ratio.

Additional legal and ethical issues arise where genomic and health-related data are made available to broad communities of users and organisations for secondary use. Sharing sensitive and potentially identifiable genomic and related-health data raises concerns about increased risk of privacy breaches, affecting the rights and interests of data subjects and their families. Countries outside the EEA may not provide equivalent legal protections or ethics oversight mechanisms. Moreover, the specific purposes, recipients of data, and associated risks cannot be fully specified at the time of an initial consent, raising issues about transparency, and about whether the consent is sufficiently informed and specific. Even where the scope of consent is made clear and understood, there are concerns about the effectiveness of oversight and enforcement mechanisms to ensure data are only used for consented purposes. In short, transparent information is needed to enable individuals to make informed decisions about cross-border access and secondary use of genomic and related health data, combined with robust governance frameworks to ensure data are processed responsibly.

1.5. Methods

We have analysed ethics literature on practical and ethical challenges raised by the process of consent in the context of biobanks, genomic/genetic research, precision medicine, genomic medicine initiatives, and clinical care (see References). In our search in the PubMed databases and other relevant specialised journals, we have privileged two types of publications:

- findings and recommendations based on empirical studies, where conclusions of the study were drawn from concretely empirical evidence (e.g. qualitative and quantitative studies, e.g. assessment of research participants' perceptions of research based on the information provided through the consent form/notice, etc.,);
- recommendations, reports, guidelines, models of consent developed by key leaders and initiatives in the field.

We have also used conclusions from project workshops organised in the course of the B1MG project as well as the 1+MG use cases. We have also reviewed GDPR requirements and European Data Protection Board Guidance (EDPB). A sample of national data protection law implementations applicable in the research and healthcare sector were reviewed and are reported in the appendix.

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[10] See 1+MG Special Subjects Policy.

2. General Guidelines – Communicating Complex Information and Documentation

Both research ethics and the GDPR require consent to be informed. For that reason, full information should be provided before consent is sought. In addition, the GDPR has requirements on transparency that apply independent of the chosen legal basis. Consequently, the affirmative action signifying consent is separated from the information provision, either as the final part of the template or – more often – as a separate form, in the following referred to as a"consent form", in particular, as there should be sufficient time foreseen between information provision and consent given. The documents provided to individuals therefore typically include an "information sheet" that clearly describes what an individual can expect when participating in (genomic) research or undergoing a genomic healthcare test or what a secondary use of health and genomic data would entail. The information sheet contains sufficient information for the individual to make an informed decision. It is then linked with the consent form to record the consent process and individual agreement. A general challenge with transparency and consent in this area is how to meaningfully communicate complex information. The following guidelines address this.

1. The information sheet and consent form SHOULD present the information concisely, using clear and plain language to promote comprehension.[11]
2. Where the information sheet becomes too long and complex, the structure SHOULD be layered, presenting the most important and legally required information first and providing additional information in optional sections.[12] Consider implementing e-consent tools that facilitate comprehension e.g., by including visualisations, hyperlinks, and self-directed review of information.[13]
3. All data protection related information SHOULD be easily found in one place (e.g., one section within the information sheet) and not mixed with other information such as on the research performed.[14] Some information is highly relevant from both a research ethics and a data protection perspective (such as information on purposes, data types, categories of recipients, withdrawal rights). A layered structure permits key ethics and data protection information to be prominently presented first, with references to a subsequent section covering all data protection aspects.
4. Information that is relevant only for some purposes or some data types (e.g. legal basis, international transfer, retention time) SHOULD be provided in relation to these purposes.[15]
5. The cultural, linguistic, and socio-economic context SHOULD be considered when preparing information sheets and consent forms (e.g. religious beliefs that may not accept certain types of genetic/genomic tests, potential for stigmatisation of vulnerable groups, etc.).

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[11] GDPR Rec 58; Art 13; Art 7 - where consent is the legal basis; EDPB 05/2020, para 60.

[12] EDPB 05/2020, para 69.

[13] GDPR Rec 58.

[14] Article 29 Working Party, Guidelines on transparency under Regulation 2016/679, paras 8, 11, 33. This includes information on the identity of the controller, data protection officer (DPO) contact, categories of data, purposes, recipients or categories of recipients, etc.

[15] EDPB 05/2020

6. The information sheet SHOULD explain basic concepts such as genomic versus genetics, biosamples, genomic data, genetic variants, precision medicine, genomic research, biobank, data repository, coding.[16]
7. Consider involving community groups to ensure such issues are appropriately communicated in the documents.
8. The content of information sheets and consent forms provided to the participants may change over time. Where such changes happen, both the information sheets and the consent forms should have version numbers or other equivalent identifiers to allow referencing the other. It MUST be possible to easily establish which information was provided to the individual and what consents were obtained.
9. The consent form MUST demonstrate confirmation from individuals that they have read and understood the information sheet, and/or that the content was explained to them (e.g., as a tick box). Where different versions of the information sheet exist, the consent form MUST reference the version of the information sheet relied upon. The consent form SHOULD obtain confirmation that the individual had the opportunity to ask questions prior to signing the form.

3. General Guidelines – Processing Data for Multiple Purposes

Depending on the context, transparency information and the consent form may need to cover multiple purposes, e.g.,

a. the initial research project/healthcare test,
b. making data available through a repository for research (where specific research projects cannot be fully identified at the time of recruitment); and
c. making data available through a repository for healthcare secondary use

In such cases:

1. The information sheet SHOULD clearly distinguish the sample and data collection, the subsequent sample and data processing[17], as well as risks and ethical issues[18] associated with each purpose for which data are processed[19].

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[16] See e.g., US National Institutes of Health, "Fact Sheets"; Torpy JM, Lynm C, Glass RM. Genetics: the Basics. *JAMA.* 2008;299(11):1388. doi:10.1001/jama.299.11.1388.

[17] GDPR Art 13(1)(c).

[18] This approach is consistent with the fact that study subjects will have the option to participate in the primary purpose while opting out of making data available in the repository. A full description of the primary purpose should include the identity and location of any partner organisations participating in any project-specific data sharing. Additional considerations for genetic research include the following: In order to avoid any misconception or confusion for the research participant as to the purpose of research and the expected clinical relevance of its results, explain what is different about a genomic research project as compared to a classical clinical trial (e.g., not to evaluate a treatment but to better understand the cause and mechanisms of the participant's condition). Indicate if the research project requires recruitment of family members (e.g., for direct collection of their genomic or health-related data), why this is necessary, and if so, how family members will be recruited (e.g., asking participants' help to identify and/or initiate contact with relatives).

[19] The primary purpose may involve different categories of risks e.g., risk of injury from physical research interventions; privacy breach from the collection, storage, use, and sharing of samples/genomic and

2. The consent form MUST give individuals separate choices to agree on each purpose.[20]
3. Consider using separate consent forms or even consent processes for primary and secondary use purposes. Some overview may be needed to make the big picture clear. If a single consent form is used, consider using separate sections corresponding to the different purposes.

4. Information about Making Data Available through a Repository for Future Research Projects

While there may be different collection and recruitment contexts, the central focus of these guidelines is prospective recruitment contexts where the (or one of the) intentions is making data available through a repository to be accessed (cross-border) and used as part of future research projects. The key challenge here is how to satisfy transparency obligations when the details of future research projects cannot be fully identified at the time of recruitment. Considerations specific to consent and to processing for multiple purposes are addressed in later sections.

4.1. Information around the Purpose: the "What", "Why", "Who" and "How" of Data Sharing for Future Research

1. The information sheet MUST state that genomic and related-health data will be **made available through a repository** for health and biomedical research.[21]
2. The data protection section MUST mention the **identity of the controller** (the initial data collecting organisation) and the contact information of its data protection officer (DPO) [where applicable] responsible for the transfer to the repository.[22]
3. The data protection section MUST mention the **legal basis** for the controller's processing (all or part) of the individual's personal data to make it available through a repository for future research projects.[23] This purpose/legal basis MUST be distinguished from other purposes/legal bases.[24] The legal basis should also mention on which basis the processing of genomic and health data is legitimised (i.e. consent or the national / EU legislation).[25]

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related-health data as part of the primary research project (unauthorized access and re-identification, leading to potential discrimination, stigma, or worry). As genetic/genomic information might contain health information about biologically related family members, the privacy risks for members of the family should be explained. In terms of psychological risks, genetic/genomic data may reveal information about possible family relationships, including non-paternity; indicate that some individuals would find this information distressing.

[20] GDPR Art 7(2)(b) - where consent is the legal basis. CIOMS 2016 Guidelines.

[21] GDPR Art 13(1)(c); Art 6(1)(a) - where consent is the legal basis.

[22] GDPR Art 13(1)(a),(b). For the DPO contact information, a general DPO office is preferable to an individual who may change. To avoid confusion, it is preferable to highlight that the DPO is generally responsible for matters related to data protection, as opposed to scientific aspects of ongoing studies.

[23] GDPR Art13(1)(c).

[24] E.g., legitimate interests (Article 6(1)(f)) for archiving part of the data needed to establish audit trail and ensure reproducibility of research studies already conducted; Compliance with the law (Article 6(1)(c)) or Vital Interest (Article 6(1)(d)), when reporting of certain health-related findings are foreseen; etc.

[25] Art. 29 Working Party, Guidelines on transparency under Regulation 2016/679

4. Given that the details of future research projects cannot be fully identified in the information sheet at the time of recruitment, it is justified to use indefinite language (e.g., may) where necessary, as long as this does not undermine the fundamental rights of data subjects.
    a. The information sheet SHOULD describe the **types of research questions** the data will be used to answer in the future in a general way, as well as the processing operations already known at the time of consent, such as data collection, generation, curation, storage in a repository, and making data available to researchers (as outlined in the repository/biobank plan). [MUST where consent is the lawful basis].
    b. The information sheet SHOULD specify a **well-described area of research** (e.g., precision medicine research to better understand, prevent, and treat disease).[26] [MUST where consent is the lawful basis].
5. The information sheet SHOULD explain the reasons for data sharing and the **expected benefit for the society**, (e.g., to enable qualified researchers across the EEA and around the world to collaborate, check each other's results, and ask new questions, which can accelerate research, helping us to better understand and address disease).
6. The information sheet MUST describe **how access is provided** (e.g., in a secure processing environment) and what the **governance mechanisms** are (e.g., review and approval by a data access committee). Please note that the 1+MG governance mechanisms are still under development and recommendations for clauses can only be provided at a later stage. *Note: this requirement cannot be fulfilled without more details on the 1+MG infrastructure and governance.*
7. The information sheet MUST identify the **controller for the access provision** and specify the **legal basis**.
8. The information sheet SHOULD explain that general research results of future studies will be **published in academic journals** and presented at conferences.

4.2. Information on Recipients

1. The information sheet MUST state that data will be transferred to and **hosted in a data repository**. The name and location of the entity responsible for providing access to data for the future research projects MUST be stated (e.g., the 1+MG legal entity, if applicable).[27] *Note: this and the following requirements cannot be fulfilled without more details on the 1+MG infrastructure and governance.*
2. The information sheet MUST provide the **repository's full contact details** (legal representative; DPO) and legal basis for providing access to future users if this is not done in a separate information sheet by the repository made available in parallel.
3. Where the repository is based in an **international organisation** or a **third country**, the information sheet MUST mention the existence or absence of an adequacy

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[26] CIOMS 2016. Where consent is the legal basis - GDPR Rec 33; EDPB 05/2020, paras 155-160.

[27] Where data will be transferred to an external organisation who will act as a (joint) controller for storing and making data available for research and who plans to rely on consent as the lawful basis for this processing, the identity of the controller MUST be stated in the information sheet and consent form and the legal basis for access provision specified.

decision by the Commission or reference the appropriate or suitable safeguards and the means by which to obtain a copy of them or where they have been made available.

4. The information sheet MUST state future potential **categories of recipients** that data may be shared with through the repository, e.g. *bona fide* researchers at external research organisations including academic research institutions, healthcare institutions, pharmaceutical companies, bioinformatics and health technology companies as users or IT platforms as services providers.[28]
    a. The information sheet MUST NOT limit sharing for secondary use to specific recipients only (e.g., partner organisations).[29]
    b. The information sheet SHOULD mention that users may base their processing on a different legal basis and/or may be subject to a different applicable (national) data protection law. This may curtail the scope of data subject rights (as explained below in the context of each right).
5. The information sheet MUST NOT limit the **geographical location** of recipients to certain countries within the EEA.[30]
6. The information sheet MUST state whether or not there is an intention to share data with **users or IT service providers based in third countries outside the EEA**.[31] Where the data are made available to entities outside the EEA, foreseeable transfer mechanism(s) MUST be mentioned (e.g., adequacy decision, appropriate safeguard). The data protection section MUST indicate where more specific information on the nature of the transfer mechanism can be obtained.[32] Failure to mention this may restrict data sharing to the EEA.

4.3. Categories of Samples and Data

1. The information sheet MUST describe the **types of data** that will be made available for secondary use (e.g., demographic data, clinical data, genetic data, in case of 1+MG, whole genome, family health history, lifestyle, mobile health data etc.) either by default or additionally on request.[33]

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[28] The 1+MG Data Governance Policy requires that access to data for secondary use be provided on a non-discriminatory basis. This recommendation is driven by the general ethical and legal principle of non-discrimination applied to data sharing, as well as the principle of maximizing the benefit of research participants' contributions. Especially in the case of publicly funded sequencing and the use of publicly funded infrastructure, access should be made available to any qualified and trustworthy researcher able to advance science. Data protection compliance processes should not be designed to lead to the de facto proprietary treatment of data. Practically speaking, necessary recipients cannot reasonably be predicted in advance for precision medicine research. For public bodies who will be subject to the proposed *Data Governance Act*, non-discriminatory access will be a legal requirement (Art 5).

[29] If you plan to rely on consent as a legal basis, however, ensure your national law or regulations do not require the identity of all recipients to be specified (Rec 42).

[30] Note there is no legal requirement to mention cross-border access within the EEA, though there is nothing wrong with explicitly stating this.

[31] The 1+MG does not foresee enabling access to researchers in third countries outside the EEA without equivalent privacy protections, as derogations (e.g., consent) are exceptional (GDPR Art 49).

[32] GDPR Art 13(1)(f).

[33] GDPR Art 14(1)(d), GDPR Recital 61Council of Europe, Convention 108, Art. 8(1)(c)

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2. The information sheet MUST also describe the **categories of biological samples** that may be made available through the repository (e.g., blood, saliva, tumour tissue), either by default or additionally on request. The information sheet MUST explain that these samples may be used to create additional molecular data.[34]
3. The information sheet MUST clearly describe the categories of existing biological samples and personal data that will be obtained from **existing sources** and those sources are (e.g., samples accessed from existing biobanks, data collected in the context of medical care, and linkage with electronic health records) and specify the **categories of data providers** (e.g., medical centres, government databases). Clarify in particular if linkage to electronic health records will be obtained periodically, and if so, over what period of time.[35]

4.4. Duration

1. The information sheet MUST mention for **how long** the data (and, where applicable) samples will be made available through the repository for future research. This can be either an absolute timeframe or criteria for how long data will be kept (e.g. relevance for future research). In the latter case, the information sheet SHOULD also provide information how these criteria will be monitored. In addition, a possible time horizon SHOULD be given.
2. The information sheet MUST mention if different timeframes and/or criteria for archiving apply that may require storage beyond the active availability.
3. The information sheet MUST mention what happens to the data at the end of the retention period (i.e. erasure, anonymisation).

4.5. Re-contacting Data Subjects

There are a number of reasons why the data subjects may be re-contacted. Re-contacting in the context of the data reuse is for the interests of the entity providing data to the users' research projects, i.e. 1+MG, as well as the data users themselves. However, contacting channels may be defined on a national or local level and could involve the data holder. It is important that the data subject has the possibility to consent, opt-in or opt-out in an informed way to the data transfer to the 1+MG repository but also that if, optional processing in the 1+MG repository might result in re-contacting, a separate informed decision can be taken by the data subject. Therefore, the information sheet MUST explain when and why re-contact may happen.

4.5.1. Re-contacting Related to a Specific Research Reuse

Transparency requirements of the GDPR mean that data subjects must be informed about any purpose that their data are processed for. In the case of data sharing for secondary use, the

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[34] GDPR Art 14(1)(d).
[35] GDPR Art 14(1)(d).

entity providing data to users as well as the users themselves have information obligations towards the data subject about the specific purpose that the data are used for. This information is essential for data subjects to be able to object to the processing in time. Where the data were not obtained from the data subject directly, Art. 14(5)(b) GDPR permits alternative methods if provision of information directly to the data subject involves a disproportionate effort. However, where re-contacting is foreseen also for scientific reasons, no disproportionate effort may be justifiable as mechanisms and procedures for contacting data subjects are in place. In such cases, 1+MG will provide information on each new purpose following an access decision. Different channels and frequencies / time points to provide this information MAY be possible and SHOULD then be described as well as a choice given between different options where possible.

1. The information sheet MUST explain how detailed **information about future research projects** will be offered/made available to the data subject (e.g., direct communication; website, and/or on request). Where direct communication is possible, the data subject MUST be given a possibility to be informed about each new access in advance. The data subject SHOULD also be able to choose only periodic information or passive information options where information can be found on demand.[36] In case of passive information or aggregated information on data use, the information sheet MUST warn the data subjects that an objection may not be possible in all cases once the research has started.
   Note: this requirement cannot be fulfilled without more details on the 1+MG infrastructure and governance.
2. The information sheet MUST (where applicable) mention the possibility of future contact to **collect additional samples/data** (e.g., as part of future research projects) or to participate in clinical trials.
3. The information sheet SHOULD (where applicable) mention the possibility of future contact to **seek renewed consent** (e.g., where necessary because of a substantial change in the scope of research aims supported by the repository or where technologies for analysing samples/data substantially change in an unanticipated and material way).[37]

4.5.2. Re-contacting to Return of Findings of Individual Health Relevance

Organisations who collect and/or generate genomic and related health data are normally required to have a plan in place for handling different kinds of findings with health relevance for individuals or their relatives as part of the primary purpose *(e.g., research project/healthcare test). Findings of individual health relevance may include individual research results linked to the aims of a research project, or incidental findings outside the*

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[36] EDPB 05/2020 para 161 “A lack of purpose specification may be offset by information on the development of the purpose being provided regularly by controllers as the research project progresses...”. Consider if national law or authoritative guidance requires direct notification of data subjects in advance of processing for any specific research project, i.e., in advance of granting access (Art 13(3)).

[37] CIOMS 2016

aims of a research project/healthcare test. For recommendations about how to handle findings of individual health relevance, see the 1+MG Incidental Findings Policy. In case of secondary use, it should be clarified to which extent the same policy will also be applied or if incidental findings may be handled differently. In 1+MG, only clinically actionable findings will be reported. This needs to be considered and may deviate from policies applicable to the primary purpose. Here, best practice suggests that these policies SHOULD already be described in the information sheet for the primary purpose of data collection or processing, or, if not applicable there, or if the policy is different to the proposed processing in the 1+MG, then it SHOULD be described in the 1+MG information sheet. These consent recommendations should also be sufficient to cover the handling of incidental findings from secondary use.

1. The information sheet MUST state if the same incidental finding policy as for the primary purpose will apply. Where this is not the case, the elements MUST be addressed where they differ from the original policy:
2. Explain whether or not findings of individual health relevance found through the secondary use will be reported to participants and/or their families.
3. Explain where applicable if these findings will be limited to individual results related to the primary aims of sequencing or incidental findings beyond the primary aims of sequencing.[38]
4. Explain the conditions under which findings of individual health relevance will be reported to participants and/or their family members e.g.,
    a. the level of clinical significance (e.g., life-saving, clinically actionable),
    b. the level of validation (e.g., in an approved genetic laboratory), and
    c. the time period (e.g., data use in 1+MG could go over decades).
5. Offer participants the choice not to receive findings of individual health relevance, and explain any situations where preferences may be overridden by professional obligations (e.g., where there is a legal duty to warn family members of life-threatening conditions).
6. Describe the procedure for how findings of individual health relevance may be returned (e.g., reporting through a designated medical professional). Note that procedures in 1+MG may indeed be different to procedures for incidental findings in the original collection context.
7. Explain if findings with shared health implications for biological relatives will be reported to them, and under what conditions (e.g., only with the participant's consent, potential obligation of the participant to inform relatives, or only after the participant's death).
8. To avoid therapeutic misconception, reiterate that the possibility of receiving individual findings of health relevance should not be equated with diagnostic testing or screening.

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[38] Note our recommendations for a 1+MG Incidental Findings policy consider all findings of individual health relevance in secondary use contexts as "incidental findings", and that any return of such findings through 1+MG should respect the initial plan and consent established at the time the data were collected.

4.6. General Communication on Research Results and other Information

1. The information sheet SHOULD [where personal communication such as email is used: MUST] explain how the general research results of future studies will be communicated to participants (e.g., list of publications on the data repository website, subscription newsletter, or upon request).

2. Where applicable, data subjects MUST be given a choice if they want to receive newsletters about general research results and other matters related to the 1+MG initiative. In this case, the legal basis for the communication MUST be mentioned.[39] If legitimate interest is chosen as the legal basis for the processing of personal data in the context of information provision, the interest MUST be explained in the information sheet.

Note that communication channels to inform about 1+MG and general research results are still subject to development and a final decision in 1+MG.

4.7. Voluntary Participation and Right of Withdrawal of Consent or Objection to the Processing

1. Individuals MUST be informed that making their data available through the repository is entirely voluntary, and that they may discontinue participation at any time, without any penalty or disadvantage by objecting to the processing [where opt-out is the basis of inclusion] or withdrawal of consent [where the legal basis is consent or where an opt-in is obtained].[40]
2. [Where consent is the legal basis for the sharing with and/or from the repository] The information sheet MUST explain that a withdrawal of consent means that the data will not be hosted anymore for future research but that it does not affect the lawfulness of the data sharing that has happened already.[41]
3. The information sheet MUST provide instructions on how to withdraw from participation in the repository, to withdraw consent or object to individual purposes or otherwise exercise rights (e.g., contact the research team).[42]
4. The information sheet or information provided at the time of withdrawal MUST offer separate choices to withdraw[43] from (where applicable):
    a. individual research projects;

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[39] Directive 2002/58/EC (ePrivacy Directive) only requires consent to unsolicited emails for marketing in Art. 13. The information on 1+MG is not marketing any products or services. Therefore, a consent is not necessarily required. However, if no other legal basis under Art. 6 GDPR applies, consent rather than opt-in will have to be sought.

[40] GDPR Art 7(3) - where consent is the legal basis. CIOMS 2016 (2). To respect this requirement, any withdrawal process must separate choices to withdraw from the primary purpose, the purpose of precision medicine research, and other purposes (e.g., secondary healthcare use).

[41] GDPR Art 13(2)(d), Art 14(2)(d).

[42] EDPB 05/2020; GDPR Rec 39.

[43] GDPR Rec 43.

    b. future active participation/ provision of data (e.g., continuing to undergo physical procedures, site visits, providing longitudinal survey or mhealth data as part of a Cohort study);
    c. future linkage to electronic health records (e.g., as part of a Cohort study);
    d. contribution of data types not required as part of the minimum dataset of the repository;
    e. the continued storage, sharing and use of already collected data and/or biological samples in a repository/biobank; and
    f. contact in the future (per purpose as specified in the consent form).
5. The information sheet SHOULD indicate what would happen to data and/or biological samples should they withdraw from the repository (e.g., samples/data will be destroyed and/or anonymised).
6. The information sheet MUST explain and justify limitations on the right to withdraw from research projects for which data were made available by the research repository, namely where this would jeopardise the integrity of ongoing or archived research projects:
    a. It may not be possible to withdraw data that is already being accessed as part of an ongoing research project where this is not feasible for practical reasons or would seriously impair the research.[44]
    b. it will not be possible to withdraw data from a completed research analysis.
    c. it will not be possible to withdraw data archived after completion of a research project for the duration of the archiving period, to ensure the integrity of completed research projects.

4.8. Other Applicable Rights

1. The information sheet MUST indicate **how** data subjects can exercise their rights (e.g. contacting the research team or through a dedicated tool).
2. [Where there is an **intention to destroy the pseudonymisation table**] The data protection section SHOULD mention that it may not be possible to exercise data subject rights where the link back to the individual's identity is no longer retained.[45]
3. **Right to rectification.** The information sheet MUST explain that data subjects have the right to request correction of inaccurate personal data and the completion of incomplete personal data, but that this right may be limited where necessary to achieve research purposes.[46]
4. **Right of access**
    a. Access to information. The information sheet MUST explain that data subjects have the right to access information on how their personal data is being used and shared, including the purposes of approved, ongoing, or completed

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[44] There may be exceptions where data is not kept in an identifiable form (GDPR Art 11), or where consent is not the legal basis. Even where consent is the legal basis for collection and storage, and for the collecting organisation's research projects, the research organisations accessing pseudonymised data may not rely on the same legal basis and thus the right to withdraw consent to processing will not apply.

[45] GDPR Art 11.

[46] Art 89(2) derogation where provided by Member State law (in one or more countries).

    research projects, the categories of personal data and the identities of the recipients involved (e.g., names of the institutions and/or principal investigators), and the existence of any international transfers and the associated legal mechanism, etc.. Explain that this information will be available on request, and may be available through additional means (e.g., website, by subscription to a periodic newsletter, regular notifications about new projects). Where applicable, explain if national or EU legislation, the right to access is limited for public sector bodies.

    b. <u>Access to a copy of personal data</u>. Explain that data subjects have the right to access a copy of their personal data[47], but (where applicable) that this right may be limited where necessary to achieve research purposes[48], where other laws restrict communicating genetic or health data (e.g., genetic testing laws) or where the data may interfere with the privacy of others (e.g., genetic information of relatives). When assessing the potential applicability of these limitations, it MAY be helpful to distinguish between access to the following types of personal data:
        i. Data directly provided by the data subject. This includes: contact information, past medical history details, answers to questionnaires, measurements done directly on the patient.[49]
        ii. Data generated by virtue of the data subject's participation in research or undergoing the initial medical procedure. This includes raw genomic sequence data and any other data derived from biosamples.[50] Consider mentioning available formats for raw whole genome sequence data include e.g., BAM, VCF.
        iii. Data inferred by analysing the raw data (individual research results).[51]

5. **[Where consent is the legal basis for the data hosting in the repository] Right to data portability**. The data information sheet MUST explain that the individual has a right to receive the personal information *they have provided directly* in a structured, commonly used and machine-readable format, or to have the information transmitted to another organisation without hindrance.[52] Data provided directly includes those listed under (i) above, but does not typically include data generated from samples. Mention that the right does not apply beyond the data directly provided by the data subject, to the original controller.

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[47] Art 15(3).

[48] Art 89(2) provides the possibility of a derogation where provided by Member State law. Consider if the limit relating to risks to third parties applies, though this seems unlikely in this context (Art 15(3)).

[49] This data MUST always be made accessible when consent is used as the legal basis. (Art 20 GDPR).

[50] In some cases, there may be national laws in place prohibiting the disclosure of genomic data outside the context of genetic counselling. The consent form must clarify if such additional conditions apply.

[51] This includes the analysis and interpretation of raw genomic data. (Providing access to this type of data is optional regardless of the legal basis, and should be based on the data controller's policy on the return of health-related findings).

[52] Art 20.

6. The information sheet MUST explain that data subjects have the right to **lodge a formal complaint** with the competent Data Protection Authority (DPA); specify the relevant DPA the data subjects can contact for this matter.

4.9. Risks

1. The information sheet MUST explain that sharing data with researchers from external research organisations may increase the **risk of privacy breaches**, especially considering there is always some risk of being re-identified from genomic and related health information.[53]
2. The information sheet MUST explain the potential **consequences** of such risks.
3. The information sheet SHOULD explain that ongoing progress in science and technology such as artificial intelligence makes it possible to perform **unanticipated forms of research** that may turn out to be controversial.
4. The information sheet SHOULD mention the potential risks of sharing data with **recipients in third countries or international organisations** with potentially lower privacy protections [where applicable]. [This is a MUST where consent is the legal basis.][54]

4.10. Safeguards

1. The information sheet MUST describe in general terms the kinds of **safeguards** that will be adopted to protect personal data and/or biological samples (without being too specific so as to limit changes in the future).[55] E.g.,
    a. data pseudonymisation, meaning all direct identifiers (such as your name, address, data of birth, ID number) will be stored separately and replaced with a unique identifier making it hard to trace the information back to you.
    b. only controlled and managed access to secure data repositories is given to qualified researchers, with access being subject to monitoring and auditing.
    c. data access/use agreements for accessing parties limiting their use to pre-approved purposes (e.g., specific studies) and requiring them to refrain from deliberately identifying individuals.
    d. access to data and research projects will be subject to appropriate oversight by a data access committee and/or a competent research ethics committee.[56]
2. The information sheet MAY inform where/how more **precise descriptions of safeguards** and/or the data protection impact assessment can be found.[57]

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[53] GDPR Recital (39).
[54] GDPR Art. 49(1)(a).
[55] GDPR Recital 39.
[56] CIOMS 2016 Guidelines.
[57] WP29 Guidelines on Data Protection Impact Assessment (DPIA) and determining whether processing is “likely to result in a high risk” for the purposes of Regulation 2016/679.

3. The information sheet MUST mention limitations of safeguards and remaining risks.[58]
4. Where data are transferred to **third countries or international organisations**, the information sheet MUST reference the appropriate or suitable safeguards and how to obtain a copy of them or where they have been made available.[59]

4.11. Benefits and Commercialisation [ethical requirements]

1. The information sheet SHOULD explain that the main aim of research is **scientific progress**, i.e., to advance our understanding of disease and that the research may range from basic research to applied research. Ultimately, this could lead to new approaches and products to prevent, diagnose and/or treat people with a similar condition.
2. The information sheet SHOULD explain, where applicable, that research aims at general knowledge and that inclusion in the repository is **not likely to benefit the individual and/or their family members directly**. In some rare disease cases, diagnosis of individuals and families may be a clear goal and foreseeable outcome for the inclusion in the repository.[60]
3. The information sheet SHOULD explain that research results may lead to **commercial products**, and that the individual will not have any monetary rights in these products.[61] It may be helpful to provide illustrative examples, such as drugs, clinical decision support systems, etc.

5. Consent to Making Data Available through a Repository for Research

1. For data that are obtained in a **research context**, an **opt-in** as informed consent MUST be obtained unless a waiver is given by a competent ethics committee. For data collected in the healthcare context, at minimum an opt-out MUST be offered. The separate consent MUST repeat key elements of the information as described below.

1. Where the consent form is a separate document from the information sheet, the consent form SHOULD mention that information has been received and refer to the **versioning of the information sheet** where applicable.
2. Consent as opt-in MUST be connected to an **action by the data subject** such as a tick box.
3. The consent form MUST **repeat key elements of the information** material to an informed decision including: the **controller** to whom consent is given for the transfer; the aim of **making data available in a repository** for future research projects in a well-described area, **hosting of data** in a particular repository, **potential access** by researchers at external research organisations, the **types of data** made available (e.g.,

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[58] CIOMS 2016 Guidelines; GDPR Recital 39.
[59] GDPR Art. 13(1)(f).
[60] CIOMS 2016 Guidelines (11).
[61] CIOMS 2016 Guidelines (11).

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health and WGS), and the s**cope of potential transfers to third countries**. These considerations are of particular relevance where consent is the legal basis for processing, but may also be relevant where an ethics consent is obtained.

4. The consent form SHOULD consider giving individuals the option to **limit their consent to a narrower area of research** where this choice is likely to allow certain members of the recruitment population to respect important personal preferences (i.e., disease-related research limited to their own disease group).[62]
5. [Where consent is the legal basis] The consent form MUST mention the **possible risks of transfer** to the repository if it is based in a third country or an international organisation and there are no appropriate safeguards as described in Art. 46 GDPR or adequacy decision in place.[63]
6. [Where consent is the legal basis] The consent form MUST mention that the data subject has the right to **withdraw consent** at any time.[64]
7. Concerning information about specific data use (sharing for defined projects) according to Art. 14 GDPR: ideally data subjects could be given a **choice how** they want to receive information: active messages in each case, regular summaries or passive information only.
   Where such choice is applicable, data subjects SHOULD be able to select the preferred way of communication and/or (independently) the timing. A warning SHOULD be added that after the commencement of a research project, an objection may not always be possible.
8. The consent form MUST (where applicable) offer **separate choices for contacting** the individual in the future:

    a. for the purpose of reporting **findings** of individual health relevance;
    b. for the purpose of requesting **additional data** and/or biosamples;
    c. for the purpose of **recruitment into future studies** requiring active participation (e.g., precision clinical trials);
    d. for the purpose of providing **general information** about the repository and the general research results achieved with the data.

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[62] If such choices are given, these categories SHOULD be aligned with a controlled vocabulary of administrative (rights) metadata across 1+MG, to ensure both that individual consent and choices can be tracked and enforced, and also that data can be meaningfully integrated and re-used. See e.g. GA4GH Machine-readable Consent Guidance, coding the GA4GH Data Use Ontology.

[63] GDPR Art. 49(1)(a); EDPB Guidelines 04/2020.

[64] GDPR Art. 7(3); EDPB Guidelines 04/2020.

References

Regulatory Guidance

EDPB, Guidelines 05/2020 on consent under Regulation 2016/679 at https://edpb.europa.eu/sites/default/files/files/file1/edpb_guidelines_202005_consent_en.pdf

Guidelines and Reports

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Examples

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