

4. Informed Consent

Obtaining informed consent specifically for the purpose of donating DNA for large-scale sequencing raises some unique concerns. Because anonymity cannot be guaranteed and confidentiality protections are not absolute, the disclosure process to potential donors must clearly specify what the process of DNA donation involves, what may make it different from other types of research, and what the implications are of one's DNA sequence information being a public scientific resource.

Federal regulations (45CFR46 and 10CFR745) require the disclosure of a number of issues in any informed consent document. They include such issues as potential benefits of the research, potential risks to the donor, control and ownership of donated material, long-term retention of donated material for future use, and the procedures that will be followed. In addition, there are several other disclosures that are of special importance for donors of DNA for large-scale sequencing. These include:

- the meaning of confidentiality and privacy of information in the context of large-scale DNA sequencing, and how these issues will be addressed;
- the lack of opportunity for the donor to later withdraw the libraries made from his/her DNA or his/her DNA sequence information from public use;
- the absence of opportunity for information of clinical relevance to be provided to the donor or her/his family;
- the possibility of unforeseen risks; and
- the possible extension of risk to family members of the donor or to any group or community of interest (e.g., gender, race, ethnicity) to which a donor might belong.

Many academic human genetics units have considerable experience in dealing with research subjects and obtaining informed consent, while the laboratories that are likely to be involved in making the libraries for sequencing have, in general, much less experience of this type. Therefore, library makers are encouraged to establish a collaboration with one or more human genetics units, with the latter being responsible for recruiting donors, obtaining informed consent, obtaining the necessary biological samples, and providing a blinded sample to the library maker. Collaboration with tissue banks may be considered as long as these banks are collecting tissues in accordance with this guidance. The library maker should have no contact with the donor and no opportunity to obtain any information about the donor's identity.

5. IRB Approval

Effective immediately, projects to construct libraries for large-scale DNA sequencing must obtain Institutional Review Board (IRB) approval before work is initiated. IRBs should carefully consider the unique aspects of large-scale sequencing projects. Some of the informed consent provisions outlined may be somewhat at odds with the usual and customary disclosures found in most protocols involving human subjects and which IRBs usually consider. For example, research subjects usually are given the opportunity to withdraw from a research project if they change their minds about participating. In the case of donors for large-scale sequencing, it will not be possible to withdraw either the libraries made from their DNA or the DNA sequence information obtained using those libraries once the information is in the public domain. By the time a significant amount of DNA sequence data has been collected, the libraries, as well as individual clones from them, will have been widely distributed and the sequence information will have been deposited in and distributed from public databases. In addition, there will be no possibility of returning information of clinical relevance to the donor or his/her family.

6. Use of Existing Libraries for Large-Scale Sequencing

Many of the existing libraries (including those derived from anonymous donors) were not made in complete conformity with the principles elaborated above. The potential risks that may result from their use will be minimized by the rapid introduction of several new libraries constructed in accordance with this guidance, which NCHGR and DOE are taking steps to initiate. This will ensure that the existing libraries will only contribute small amounts to the first complete human DNA sequence. In the interim, existing libraries can continue to be used for large-scale sequencing, only if IRB approval and consent for "continued use" are obtained⁶ and approval by the funding agency is granted.

It is important that in obtaining consent for continued use of existing libraries, no coercion of the DNA donor occur. It is therefore recommended that consideration be given to whether it is appropriate for the individual who previously recruited the donor to recontact him/her to obtain this consent. In some cases an IRB may determine that the recontact should be made by a third party to assure that the donors are fully informed and allowed to choose freely whether their DNA can continue to be used for this purpose.