CONSEJO DE INVESTIGACIÓN MÉDICA SUECO

RESEARCH ETHICS GUIDELINES FOR USING BIOBANKS, ESPECIALLY PROJECTS INVOLVING GENOME RESEARCH OF JUNE 1999

Introduction

During recent years, the Swedish Medical Research Council's (MFR's) policy-setting Committee for Research Ethics has received an increasing number of inquiries from both the research ethics committees and the pharmaceutical industry regarding the conditions for continued use of human biological material that has been collected in biobanks, particularly concerning material containing genetic information.

The questions often concern the principle of informed consent, ownership rights, or issues related to responsibility:

What procedures must be followed if a sample was submitted a long time ago and for some other purpose?

May material be used if the donor is dead, but in case relatives are affected?

Who assumes responsibility for information included in or derived from these banks?

Who has ownership rights and who has user rights?

Who will set priorities regarding the use of finite biobank materials?

Who decides about making samples anonymous?

How are code keys handled, and by whom?

Can the material be sent abroad?

Regarding the legal aspects of these problems, the MFR has requested (March, 1999) that the Ministry of Education and the Ministry of Health and Social Affairs quickly appoint a commission to review existing legislation and its application in these special issues. The handling of human material in activities closely associated with health and medical care such as evaluation and quality assurance are important to consider and should be dealt with the National Board of Health and Welfare.

There has also been intense debate in the other Nordic countries, in conjunction with projects such as the Icelandic de Code. In Denmark, the Danish Medical Research Council, together with the Central Scientific Ethics Committee and the Danish Council of Ethics, carried out a thorough investigation regarding guidelines and legislative policy about information related to biobanks. A seminar was conducted under the auspices of the Nordic Council of Ministers in Iceland in May 1997: "Human biobanks ethical and social issues".

The seminar is also documented in a series of publications issued by the Nordic Council of Ministers. Further,

the problem complex has recently been treated in an opinion of the European group on ethics in science and new technologies, appointed by the European Commission; "The ethical aspects of human tissue banking", in which a special opinion was proposed to cover such tissue banks that contain genetic material. These EU documents have thus not yet led to any convention but are in harmony with the general principles prescribed in the Council of Europe's "Convention of Human Rights and Biomedicine", which includes general ethical guidelines for biomedical research.

General Background and Problem Identification

Biobanks may be used in both broad and narrow contexts. Sometimes biobanks are used as a wide concept that includes tissue banks. It may be clarifying to distinguish among the following:

1) Tissue samples (blood samples, biopsies, sperm banks etcetera).

2) 1) Including information on those patients who submitted the samples, their diagnosis, disease, medication consumption and reaction to the medicine.

3) 2) Including information on those physicians who diagnosed and treated the patients, as well as those hospitals where the treatment took place.

4) 2) or 3) Including the information obtained from the tissue samples using different analytical methods based on genetic engineering.

5) Only this informaton (DNA-libraries, genomic libraries).

There are several reasons for trying to keep these types of biobanks separate. First of all, Swedish legislation currently only offers protection for information, not for the actual tissue samples. Secondly, these types of biobanks represent different storage and security problems. Naturally, the information obtained using various analytical methods based on genetic engineering from the tissue samples does not need to be stored at the same temperature as the tissue samples to avoid contamination, infections, destruction of the samples, etcetera.

By definition, hereditary illnesses are unique because more than one person is affected. This means problems for the traditional requirement for information and consent. Who will be informed? Who should grant consent? Does anyone involved have vetoing rights? Certain types of genome research are also characterized by the fact that cutting edge research changes rapidly. What was not possible a few years ago is practiced today. The person who consents today to allow samples to be used for future research therefore does not always know what he or she is consenting to, if unrestricted consent is granted.

Obviously biobanks involve several potentially conflicting interests that must be weighed against one another. The interests of the donor, relatives, the owner of the biobank, research, and the industry may conflict. Which requirements are reasonable to make from an ethical viewpoint to minimize such conflicts, improve protection for the patients, preserve and improve long-range confidence in the health and medical care system? Which of the common ethical demands for information and consent will cause pro-

blems? It is not easy to inform adequately and know what should be included in the information, because of rapid developments in genetic engineering. Donors should have the right to be informed about how the samples will be stored, and for how long, how they will be registered, and what will be done to prevent unauthorized parties from accessing the information, and not least, about those uses of the samples that can be predicted.

For example, these may involve diagnostic purposes, transplantation purposes, quality control development of pharmaceutical products, research, cell culture, etcetera. It is important that the donor be able to waive his or her consent at any time. As was mentioned previously, it is not easy to grasp the meaning of unrestricted consent for samples to be used for research, since the research front, the problems, and the methods progress rapidly. This could mean new roles for the ethics committees, which to a greater extent than today may have to enter into dialog with researchers and other concerned parties and in each individual case determine if consent may be presumed or if individual consent must be obtained. Other ethical aspects involve confidentiality, the right to protection of the donor's privacy and encroachment on the donor's integrity.

For biopsies to be of interest for research and pharmaceutical production, in most cases they must be combined with information about the patient's medical history, medications, reaction to medications, adverse effects, if any, etcetera. The question is what value the samples may have without any accompanying information. The more information that accompanies the samples, naturally the easier it is to identify the individuals or groups from whom samples have been obtained. The problem is what can be done in this case to limit the risk of stigmatization and discrimination of groups.

Since it must be possible to trace any marker of disease that originates from the samples, it must be possible to identify the donor, while developing a coding system to prevent anyone without authorization from accessing the information.

Confidence in the activities involved in operating biobanks is a fundamental issue. Openness and insight are cornerstones, as is correct information on prerequisites and future uses of the sample.

Research Ethical Guidelines

Against this background the MFR's Committee for Research Ethics gives the following guidelines as advice to both individual researchers and industries, as well as to the research ethics committees across the nation. The guidelines refer to the use of biobanks for research regardless of whether the samples are collected as a component of routine medical care or for previous or current research purposes. The guidelines also apply, where appropriate, when biological material is collected mainly for an identified research project.

Storage, Organization, Responsibility

All biobanks containing both biological material as well as associated information about individuals must have an organization with explicit pro-

cedures for quality assurance, including systems for storage, coding (identification and preservation of anonymity) and registration. They must also have clear conditions for responsibility and management. If biobanks are to fulfill important purposes for future biomedical research, the identity of the samples must be preserved. It is essential for biological material to be coded, and for the code key be stored separately. The code must be kept within public institutions. Strict rules for storage and the use of the code key must be established, preferably in consultation with the local personal data representative.

Conditions for Use

There are Several Prerequisites to Obtain and Use Samples for Research Purposes:

a) An application must be sent in to and approved by a research ethics committee. The ethical review should include a decision as to if and when a new informed consent is required and the conditions under which the code may be broken.

b) A special scientific review is required when only a limited supply of the material is available.

a. *Research Ethics Review.* All research projects that intend to use human biological material must be reviewed by the research ethics committee, even if the material in question has already been collected. The application must clearly state whether genome analyses will be conducted and/or whether a biobank will be built up. The application must include a special description and comments regarding this part of the study. The research ethics committee must particularly consider the following regarding informed consent:

i) Informed Consent for Storage. Informed consent for each new purpose is the main rule, which means that general information where the patient consents to the use of collected material for unspecified future research cannot be accepted. Anyone who collects biological material and associated information about individuals that will be stored must obtain informed consent for this. The information must include details about storage procedures, storage time, and the person in charge of the biobank. In addition, it must be clear that the material may be used for future research, which in such case will be reviewed and approved by the research ethics committee, and that the donors may be contacted again. Further, the donors must be informed of the possibility that their samples may be destroyed at any time on their request.

ii) Informed Consent for New Purpose. Assuming that the benefits of the knowledge to be gained are judged to clearly outweigh the risk for violation of integrity of individuals or groups of individuals, the research ethics committee may depart from the main rule of new informed consent in certain cases. There may be reason to test whether conditions for such departure are present, as in the following cases: a) if only strictly coded material is used; or b) the purpose, problem, and type of analysis in the new research project are very close to the one about which the subject has been informed previously and to which consent has been granted; or c)

if such a large number of individuals is included in the study that individual informed consent in reality would make the study impossible. In such cases providing information through advertising may be considered and the "opt out" principle would be in effect (if a person has not said no, then the person had said yes). The research ethics committee must also carefully consider situations such as when gene markers may have individual or group interest for concerned relatives of the person who has submitted the sample.

In such cases informed consent should be obtained from anyone who could be directly affected by research results.

iii) Deceased. In those cases where previously collected material is intended to be used and some of the donors are deceased, the research ethics committee must determine whether relatives of the deceased should be informed or not. If relatives are to be contacted the project manager must clarify how the relatives would be traced, how they would be informed and, if relevant, how they would be taken care of and who would be responsible for this.

iv) Code Keys. The research ethics committee will determine under which premises code keys may be used when the material is to be used for research. The research ethics committee must thereby take into consideration the fact that the code may be broken not only to ensure an important research interest, but also at times to ensure the individual's interest if, for example, the research can identify a marker for a disease for which some form of intervention may be available.

b) *Preservation of Materials of Limited Supply.* Universities and county councils should assume responsibility to ensure that the biobanks they handle can be preserved for future research; that is, they should not be permitted to run out of materials. It is reasonable that the researcher(s) who started a research project that led to the creation of a biobank in the first place has (have) the right to use the samples for the original project. After that the use of such material will become the object of special scientific review and priority setting.

Profit interests for such biobanks that are publicly operated must not influence scientific evaluation. Further, basic research interests must be weighed against interests from applied research, and research regarding common diseases must be weighed against interests regarding unusual diseases. If the material is collected for clinical purposes and the material may have significance for such purposes in the future, these must be given precedence.

Biobanks in Industry

Rules on research ethics review should apply in the same manner for biobanks maintained within industry. Such biobanks should only include coded material. A code key should be stored with a suitable public authority such as a university or county council.

International Collaboration

In the case of international collaboration, only coded material may be sent abroad. If the information is sent

abroad the personal information act must be observed. When Swedish researchers use tissue samples from foreign biobanks or donors, and if the project is initiated in Sweden or is financed with funds from Swedish grants, the project must also be reviewed by a Swedish research committee along side of existing rules in each country. See also "Guidelines for ethical evaluation of medical human research – research ethics policy and organization in Sweden", MFR Rapport 2, 1966, pages 41-42 (available in English edition 1998).

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