

In the interests of efficiency and integrity

Mats G. Hansson

Research Program Ethics in Biomedicine, Uppsala University

The dual interests of the citizens

As can be seen from interviews in Jens Laage-Hellman's study in this project, there is a great deal of interest among scientists, pharmaceutical companies and public authorities in proposing legislation regarding the storage and use of human tissue samples. However, before this can be done it is necessary to identify the values at stake, values that the new legislation is expected to protect. The balancing of values has to acknowledge that different values are at stake for different parties. There is a pluralism of values as regards what patients, research subjects, authorities, the medical profession, scientists and the general public believe to be at stake. For some individuals, the most important values at stake are privacy and integrity. They would accordingly prefer legislation which strongly protects these values. Other individuals believe that biobanks should be used in the most efficient way possible, in order to generate new knowledge for diagnosis and medical treatment. For them, legal and ethical measures made too rigidly may actually be detrimental to the values, such as health and wellbeing, that they want to protect or promote. Overprotection could damage the public interest.¹ The legislator and the ethical review boards must find a solution to how threats to integrity should be balanced against risks of not gaining new scientific knowledge and new medical treatment.

From the perspective of actual and future patients and from the perspective of scientists engaged in the sampling of tissue material and the use of biobanks for research purposes, there is a dual interest in efficiency *and* integrity which I will outline briefly in this chapter. Patients want better, more individualized treatment with better control of side-effects. This is what research using biobanks in combination with DNA-tests and medical information about patients promises. From the perspective of patient concerns about efficiency, it is important that individual scientists or companies do not get full exclusive rights of access to the biobanks. Such a policy will exclude other scientists and companies to approach the material with other questions of relevance to patient health and wellbeing. However, the efficiency concern is not enough. The information attained and used is powerful and is a concern not only of the individual who has been diagnosed but also of all genetically related individuals. There may also be third parties such as insurance companies and employers with an interest in gaining information about the diagnosed individual and his or her relatives.² Accordingly, both actual and future patients may have interests in controlling who will have access to information about them. They have integrity concerns as well as interests in efficient procedures governing the storage, use and sharing of samples.

From the perspective of the individual scientists and the scientific community there are also efficiency concerns that should be taken into consideration before a model for storage and sharing of samples and associated information is selected. With regard to retrospective material that has been collected in association with ordinary diagnosis and treatment of patients or for

research purposes, there is a finite quantity that should not be wasted on research that is of poor quality or is jeopardized by inefficient storage and documentation procedures. With regard to prospectively collected material, interests of efficiency include a concern for quality and completeness of data and selection of appropriate storage procedures. This also comes as a reminder to the scientific community of the need to find appropriate models for sharing of samples and information. Developing and facilitating collaborative research among scientists and different biobanks is in the interest of scientific efficiency and in the interest of patient needs.³ It is also crucial that researchers ask well-defined research questions and that the biobank is used as a basis for formulating as many such questions as possible.

A scientist and his group have normally the exclusive rights to the material they have collected and organized.⁴ To violate this right is to disrespect the integrity of the individual researcher. However, this is a right the creators of a biobank should not stand on too firmly, since they are also dependant on other biobanks and data produced by other groups in order to get ahead in their own research. In the long run each scientist has an interest in defending openness within a framework of acknowledging the original contribution.⁵ The Swedish National Board of Health and Welfare has in a recent report suggested that an individual has a right to have his material withdrawn from the biobank and destroyed.⁶ However, such a right would seriously endanger the quality of the biobank. An efficient use of the biological material and the to this material associated information requires that the bank and the data are as complete as possible. An option to withdraw material or information would also conflict with accepted ethical and legal procedures for the use of medical registers in research, in many respects a parallel case.

In the interest of integrity

In the recent report on biobanks from The Swedish National Board of Health and Welfare already referred to it is stated that the “integrity” of the individual must always be protected in connection with research on human biological material. The term “integrity” is not defined, however, and therefore the requirement of protecting this value gives no concrete guidance to research ethics committees or researchers organizing human biological material into biobanks. We need to know more precisely what is really at stake when the “integrity” of blood or tissue donors is at stake. The concept “integrity” is complex and forms the subject of a comprehensive study of mine in another project. However, a brief outline will be useful here as part of an ethical analysis concerning the use of biobanks.

Within the context of research ethics a first distinction should be made between a principle of protecting or respecting integrity (hereafter the principle of integrity) and the well-established principles of beneficence and non-maleficence. In planning a research project the researcher and the ethics committee try to calculate and balance the expected utility of the project against potential risks of physical and mental harm to the research subject. The researcher must do his best to control all possible short- and long-term harms associated with participating in the research project. The rule of informed consent is applied in order to let the research subject make a voluntary and informed decision whether he is willing to accept the remaining risk and participate in the project or not. The principle of integrity may be related indirectly to the interest of protecting research subjects from physical and mental harm. A third party who gains access to medical information about an individual can use this information in a way that is damaging to this individual or to his property. Indirectly, though, it is two other basic interests that the principle of integrity is designed to protect.

To be in control of access of information about oneself

Different individuals set different limits to other parties' access to knowledge about oneself, and there can be great differences in this respect between different cultures. Even within a nuclear family, spheres of integrity may vary in size. One individual may feel that his integrity has been violated when he learns that he has been observed through the window by a stranger outside. Another individual exposes himself voluntarily, even as regards intimate details of his private life. Thus, even within a given culture it is difficult to define certain standards as to what should be counted as an infringement of the integrity of individual members of this culture. It must be up to each individual to define for him- or herself where the limits should be drawn concerning other people's access to information. The principle of integrity means in this first sense that it is always the individual who shall be in control of access to information about him- or herself. This principle may be negotiated in order for the individual to take part in social life, but in striking this balance, the principle of integrity in the second sense, as described below, should be taken into consideration.

Taking the principle of integrity in this first sense into consideration, one immediately realizes that the use of biobanks in association with genetic research and the use of personal medical information involve great risks of infringement of the integrity of the parties concerned. Genetic information about one individual is by definition also a concern of genetically related individuals. In connection with a DNA-test, an RNA-test or a protein analysis, the individual examined will receive information about his genetically related relatives at the same time as he receives information about his own genetic constitution, often without their knowledge or consent. Those concerned have no control over access to the information that is handed out, and so their integrity is violated. To obtain a voluntary informed consent from all parties concerned seems very impractical, and such a procedure may also come in conflict with the right of these individuals not to know about their genetic constitution and vulnerability, if that is what they wish.

If the examining doctor instead chooses to show respect for the integrity of an individual examined who, for various reasons, does not want to communicate the information to his relatives, he will have a problem in balancing the principle of integrity against the principles of beneficence and non-maleficence. The following imaginary example will serve to illustrate this genuine ethical dilemma. Imagine a patient who visits his doctor in order to get the results from a genetic test for a cancer. He learns that he is suffering from a malignant tumor and that unfortunately the disease has now progressed beyond any possible cure. At the same time he realizes that it was this form of cancer that his brother died of five years ago. He and his brother did not have any contact for many years. Had he been tested five years ago he could have been given effective treatment, now it's too late. It does not require much empathy to see that this situation is morally reprehensible.

It is difficult to say when and how, but it is evident that a doctor's primary duty to his patient must be expanded so as also to include those whose health and wellbeing is directly concerned by the genetic information available from genetic tests on individual patients. The ethical analysis must investigate different ways of balancing the integrity principle against the principles of beneficence and non-maleficence. In most cases the problems may be handled within the ordinary bounds of family morality. Different members of a family have contact with each other and communicate vital information to each other. Especially concerning disorders with a dominant pattern of heredity, the individual members have extensive knowledge about the disease and the family history. Genetic relatives in these cases often approach the clinical team on their own initiative. However, the problem is more acute when it comes to recessive disorders

where the individuals have no such knowledge to rely on. Even with regard to dominant disorders, the situation may be very complex.⁷ The development of genetic medicine implies a closer focus on the genetic family. However, in society of today, with new family structures and a blending of different cultures, this family may be hard to locate. The social family and the genetic family seem to be out of phase in modern society and, hence, the conflict between the principle of integrity and the principles of beneficence and non-maleficence more acute.

Respect for integrity as social recognition

The principle of integrity in the first sense as a recognition of each individual's interest in having control of other people's access to information about him- or herself must also be balanced against a principle of respecting integrity in a second sense: as social recognition. It is in particular Hegel who has discussed respect for integrity in this sense.⁸ Each individual has an interest in being socially recognized and respected as a moral agent. This includes appropriate recognition of one's contributions in society and an insight into the social norms and legal rules that, directly or indirectly, influence one's ability to play the social role one wishes to. In all social contexts, whether great or small, there must be room for compromise on individual concerns but the individual member must be in a position to understand and influence the underlying considerations and the rules that govern these compromises. Hegel described in detail three different forms of social recognition: the state, civil society and the family. Many people may today be skeptical of the Hegelian version of the individual's subordination to the interests of the state, but the element of social recognition in his political philosophy has been well accepted.⁹

The two versions of the principle of integrity protect two different interests: i) the interest in controlling other people's access to information about oneself and; ii) the interest in being socially recognized as an agent and a member of a moral community. That these two interests may come in conflict with each other is evident from the experience of the research ethics committees regarding applications in the area of pharmacogenomics. In order to protect integrity in the first sense the committee may want to select a very strict procedure for information and consent with requirements of written informed consent from all research subjects. However, these requirements may in practice constitute a violation of the principle of integrity in the second sense. The conflict is apparent to anyone trying to apply the rules in the Convention on Human Rights and Biomedicine drawn up by the Council of Europe.¹⁰ Article 22 in this convention states that: "When in the course of an intervention any part of a human body is removed, it may be stored and used for a purpose other than that for which it was removed, only if this is done in conformity with appropriate information and consent procedures". Strictly interpreted, this article requires explicit informed consent to be obtained from the original donor of the sample whenever there is a new purpose .

It is well known that the response rate in association with collection of data from any larger population is 70-80 % at best. Irrespective of how skilled the researcher is in formulating questions and regardless of how many reminders he sends out, the response rate will rarely exceed these figures. If explicit consent is required for each new use of material already collected, the effect will be to reduce the scientific value of the study, since not everybody will respond. The researcher will, furthermore, not know if those not responding might have been of particular interest in the study. If the research subjects learn to know that, in order to protect their integrity (in the first sense), a research ethics committee demands such a rigid interpretation of the duty to inform and obtain consent that the scientific value of the study decreases and, accordingly, endangers the potential for providing new treatment, they may feel that their

integrity (in the second sense) is violated. They would find it too costly to exercise a right of self-determination in a decision they would gladly delegate to the members of the committees, especially in cases when the risks are of a minor nature. To be recognized as an agent in a moral community is to be able to form the social systems in a way that implies an optimal balancing of risks and benefits. Perhaps they would like an organization similar to what has been accepted in association with research using different medical registries. In these cases it is an accepted procedure to allow the Swedish Parliament to make decisions concerning the establishment of a registry of great interest for the citizens.

A responsible ethical balancing implies that the requirement of efficiency must not without good reasons triumph over the requirements of integrity. The same holds for integrity concerns. They do not represent any absolute values that can escape an ethical deliberation. Regardless of selection of information and consent procedures the researcher and the committee is responsible for the values that will not be fulfilled as a consequence of the decision.¹¹ In balancing the different interests at stake the researchers and the committees may have good use of an elaborate system of different information and consent procedures.

Three information and consent procedures

The rule of informed consent is complex as such and involves several components that must be taken into consideration when seeking approval by patients and research subjects.¹² In addition, there are difficult philosophical problems pertinent to the task of suggesting appropriate information and consent procedures in relation to the use of biobanks. First, there is the plurality of values at stake in connection with different uses of biobanks. Information and consent procedures must take into consideration the kind of use in question: i) diagnosis for treatment; ii) quality assurance; iii) clinical research and; iv) epidemiological research. Different risks and benefits are at stake for patients and research subjects in relation to these different uses depending on i) the possibility and desirability of anonymizing information; ii) the seriousness of the disease; iii) the degree of heredity and penetrance associated with a specific kind of genetic information. In some cases it is not at all possible to secure approval.

The selection of appropriate information and consent procedures must take into account the different values that are at stake in association with different research protocols. It is not reasonable that the rule of obtaining an informed consent should be the same regardless of desired level of confidentiality and estimated benefit-risk ratio. The kind of information, the way it is given, the degree of voluntariness and the format of authorization should be adjusted accordingly. What should be considered appropriate information and consent procedures may then vary along a continuum with written and oral information and a signed consent at the one end, while at the other end of the scale it should just be a matter of making relevant information available.¹³ In a separate study of this project, Lena Lundberg and Åsa Kettis Lindblad will conduct an empirical survey focusing on information and consent procedures developed in order to test the accuracy of people's understanding and perception of the risks and benefits that are associated with individual research protocols. The respondents will be asked to choose between different versions of information and consent procedures, as judged to be appropriate in relationship to the different research protocols, i.e. i) making information available; ii) informed refusal and; iii) written informed consent. In the study by Stefan Eriksson in this project, the questions about informed consent is discussed in more detail. It is our aim to suggest procedures for information and consent that are sensitive to the values at stake and of practical use for researchers and ethics committees.

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