

## DNA SAMPLING AND BANKING: PRACTICES AND PROCEDURES

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RAPPORTEURS

### Introduction

Research in the field of human genetics continues to advance rapidly and DNA sampling has become an increasingly common medical act. No other procedure intrudes more intimately upon the individual and nowhere is informed consent more sensitive. No practice in classical epidemiology carries such implications for personal autonomy, beneficence and harm, the protection of the vulnerable, nor even for social justice. Moreover, the expanded collection of DNA samples and the subsequent use of genetic information has heightened public concern about confidentiality and privacy. Consequently, right-to-privacy legislation is being enacted in many countries. But administrative or statutory provisions may both help and hinder DNA banking, for example, privacy laws may make banking of identifiable data impossible or allow DNA sample donors to refuse banking.

This plenary's presentations suggest that any statement of principles and guidelines, no matter how carefully established and far reaching, requires a vast effort of educating the lay public as well as the medical and other professions concerned in order to insure implementation. At the same time, if the acceptance of research on population genetics depends on public attitudes towards health care and research in general, it also depends on how appropriately and sensitively genetic research projects are carried out.

It appears that the issue of informed consent has become more complex as it has become easier to use DNA samples for purposes quite different from those for which they were originally obtained as Professor McEwen states and also far into the future, long after the donor's death. A consensus seems to be emerging, however. At the beginning of any project, investigators should inform the

subjects as to the following: definition of the purposes for which the samples or the results will be used, which research groups will have access to the samples, and what results, if any, the subjects can expect to receive as presented orally by Dr. Aymé. Dr. Pembrey's oral presentation also reminds us that principles of data protection and professional secrecy are to be discussed to avoid breaches of confidentiality. Likewise, the lack of formal ethical and legal regulations in current DNA banking practices, as illustrated in Dr. Verhoef's study, underscores the urgency of remedial regulatory initiatives. Citizens rely on governments to protect them and promote their health, but governments can do this only if sufficient knowledge has been acquired to guide policy. The Government in the U.K., Dr. Pembrey notes, has seen fit to intervene in the area of genetic testing with the creation of a Parliamentary Select Committee which will study, in particular, aspects of consent to testing and the protection of personal genetic data. At an international level, guidelines can carry a moral rather than a legal weight by virtue of the authority and competence of the body establishing them and they could command wide respect as Dr. Quintana points out.

In a survey of DNA banking practices in Canada, Dr. Verhoef and her colleagues examined the details of sample collection. Local institutional policies to regulate DNA banking exist, but they are not always known. Policies on ownership/control options, duration of storage and sample destruction seem to be less well known. A majority of researchers practised anonymous linkage of donors with shared samples. Most academic research centres agree that formal policies to regulate human DNA banking are desirable. Dr. Pembrey avers that in the U.K., the majority of DNA banking grew out of and was greatly facilitated by the National Health Service (NHS); most banking in the U.K. is tied to NHS clinical services which is comprised of 14-15 Regional Genetic Centres within which clinical molecular labs are found. The NHS link has allowed the DNA banking system to carry on under the umbrella of the old system, where patient information could move around quite freely, without much thought given to guidelines or regulation. Things are changing, however, creating standards for those performing the banking function as well as protecting the individual whose DNA is banked (the Parliamentary Select Committee referred to above). To assist professionals involved in banking, the Molecular Genetics Society was formed in 1988. This organization drafted guidelines in 1989 for service labs including what is now a well established quality assurance scheme. As for the United States, Professor McEwen reports that human DNA is stored for many reasons: as a service to genetically at-risk individuals or families, who may later wish them to be available for family-based linkage testing; for research purposes, such as gene-mapping studies that may require samples from many family members over several generations; for reasons unrelated to contemporary DNA analysis but potentially useful for future testing, or, still, as a matter of routine. In France, there are many different kinds of human DNA banks established with either service, or research in mind, or both. Of the 150 known banks, however, only 2 (Généthon and Cassini) are able to provide service to external users, the balance consist of private DNA collections. DNA banking has

been largely unregulated but this may change. The French government, in response to increasing numbers of budget requests from hospitals and research labs for banking facilities, set up a Working Party two years ago to study the ethical, regulatory, practical and technical issues related to this area. The recommendations addressed the need to obtain informed consent from the patients (this requirement being largely ignored under the auspices of clinical care, as opposed to research) and the lack of quality assurance in the labs i.e.. reliability of information, operational organization. Additionally, the Working Party proposed options for the reorganization of the banking system in France. The most likely scenario would be the creation of a National Council of Banks and a small number of national DNA banks. The Council would take on the role of overseeing bank audit, activity follow-up, monitoring practices, establishing a database for information sharing, advise on political issues relating to sampling and banking, and negotiate with the government for funding. In essence, Dr. Aymé relates that the use of personally identified data in the banks and in private collections raises important issues of storage, quality, safety, practice with regard to consent, ethics of access, and freedom of research versus protection of individuals. While some banks are well organized and pose little problem, others are in research labs where the facilities cannot insure either the safety of DNA samples or of computerized information. In private collections, funding is uncertain and there are many instances of lost samples. The establishment of an overarching Council could help to correct these shortcomings and establish some degree of uniformity with regard to practice and procedures.

Similarly, Dr. Quintana notes that European human tissue banks are being used in a variety of new ways. Many of these developments have unquestionable benefits but they also raise new ethical dilemmas. If these dilemmas parallel those related to organ transplants, they differ from a legal point of view. Their similarities and differences are very relevant when considering the possibility of regulation. It is worth mentioning that if most countries have legislation on organ transplants, they less often have laws regarding tissues, with the understanding that either the standards governing organs apply, or that standards aren't necessary. Some biological materials have long been covered by specific legislation, e.g. blood and its derivatives, corneas or, more recently, materials related to reproduction such as sperm, ova, and embryos. Is there a need for specific legislation on human tissues, wonders Dr. Quintana? Human health is being increasingly legislated, yet there are specific ethical matters that are difficult to solve without targeted legislation. How then should the latter be formulated? Should it build on the experience of two decades of organ transplants? Or should it view human tissues as medical devices? Dr. Quintana believes the first alternative better fulfils ethical requirements. It would seem that public awareness regarding the collection of human tissues needs to be stimulated. It is important to note that the ease with which human specimens can be obtained and DNA isolated makes the control of unethical practices correspondingly difficult.

Current banking practices have deficiencies. These point to multiple ethical and legal questions, surrounding the nature of the information given to patients, their degree of autonomy, or still the communication gaps existing between different levels of institutional decision-makers. The primary rationale for DNA banks is likely to evolve over time. Their present aim is to make aggregate and individual data accessible for medical, statistical, and research purposes. To be of value, data must be accurate, reliable and as complete as possible. To maximize their usefulness, it is sometimes essential that donors be identified, which in itself may lead to problems. Accuracy and completeness can be achieved only if the donor and the investigator are confident that the data collected are indeed necessary for the aims of the bank and that they will be safeguarded, that is, both secured against unauthorized access and not used for purposes other than those for which they were collected. To that end, formal national DNA banking policies are necessary. In the absence of explicit guidelines, the protection of individuals (and their anonymity) remains uncertain.

Informed consent: paralogism or sophism? Is it possible to obtain informed consent for all potential contemporary and future uses of a DNA sample? The explosive growth in genetic applications raises questions that were unforeseen when samples were first obtained. Moreover, it may be very useful to keep these samples: for instance, when a donor dies or, still, for retrospective studies. At the same time, asking for unrestricted use of DNA samples will render informed consent irrelevant. Due to costs, it is tempting to make as extensive a use as possible of available samples and related data. How then to update the consent? Dr. Aymé wonders whether it is ethical to study the biological material of healthy volunteers for any type of study. How then to share the material with other research teams, with a view to maximizing its usefulness? Its relative non-availability is often a consequence of conflicts of interest between research groups. Yet sharing is a major concern for patient advocacy groups. To what extent should privacy be protected, if by the same token the power to detect important risk factors drops dramatically?

The right to control information about oneself is a fundamental value in most democracies, and means for protecting privacy are in order. Human genetic research is growing and it is recommended that the collection of DNA samples within research projects take place within the framework of laws pertaining to confidentiality and research on human subjects. Whatever the protective measures decided upon for human DNA banks, they will have to strike a balance between the dictates of privacy, and the need for a better understanding of health determinants.

In the case of forensic DNA banks Professor McEwen indicates that in the United States, DNA samples are stored for a variety of reasons. Likewise, most hospital pathology labs keep paraffin embedded tissue blocks for legal purposes. Forty states have enacted statutes that authorize or require the collection of blood from convicted sex offenders and some other types of criminals. These samples are tested for their unique identification characteristics; the resulting

profiles are then stored to be used to help identify suspects in future crimes that involve biological evidence. These practices have led to a growing societal awareness regarding questions such as 1) Who can be included in forensic data banks; 2) Who should be in charge of these banks? 3) How long should labs keep DNA samples? The consent forms do not come close to covering these issues. Proceeding with limited consent or without any at all may be appropriate in some circumstances such as crime scene investigations or in health emergencies.

Informed consent involves choices and possible control by the participants over time and even after death. There are ongoing obligations for DNA bankers in this continuum, from the time of obtaining samples and testing through to identifying markers and genes with other researchers or economic partners.

Dr. Pembrey raises other problems with DNA banking, i.e. potential breaches of confidentiality and invasion of privacy. In the United Kingdom, much human genetic research is closely integrated with medical services. This close link between service and research has certain advantages. The dual responsibilities of the medical profession to both "care for" and "learn from" the families who seek help is well understood, in particular as regards the disclosure of information and the use of DNA samples for clinical services or for research. However, the link also highlights the need to distinguish between research, service, and clinical audit because of the potential consequences. For example, in regard to the health and the daily life of individuals, being informed that one has specific genotypes associated with common diseases will mean very little in practice for a long time.

Greater caution is necessary in population wide screening than in high risk group testing. But even if one recommends that research results not be disclosed and that DNA samples collected for research not be used for clinical services, Dr. Pembrey notes that not everyone accepts this and that there is no standard practice. For example, in a service setting there is no agreement on the need to obtain specific consent from a person for their DNA analysis result to be communicated to another clinical genetics centre in order to facilitate testing of a different branch of the family. Whilst mindful of the need for confidentiality within the family, information may be transferred within the National Health Service under the umbrella of "professional duty of care" to the whole family. The problem is that individuals could be faced with information they do not wish to have, or with choices both the investigators and themselves were unaware that they may have to face. Also, knowledge regarding genetic status is not limited to individuals: this knowledge has consequences for family members, especially those in the next generation. Dr. Pembrey therefore recommends "to move away from general to more specific confidentiality" in any remedial regulatory initiatives to come.

## Conclusion

The issues of practices and procedures of DNA sampling and banking revolve around what safeguards should exist for the collection and the use of

DNA samples, as well as the disclosure of information. To whom does a DNA sample belong? How can DNA banking be done in an ethical and beneficial manner, given the dangers to individual privacy and autonomy, given the lack of defined beneficial goals at this stage of our knowledge? Under what circumstances and which government agencies should allow access to DNA samples without individual consent? What do the choices mean in terms of respect for the donors, the scientific freedom of researchers, and the legal and ethical obligations of ethics boards or government agencies? These questions have become all too familiar.

The particularities of legal safeguards (or lack thereof) will continue to differ from country to country. However, most people recognize that it is time to re-examine their parameters, given the context of a rapidly expanding capacity for genetic identification and because genetic information raises issues that go beyond strict medical information. Whether it be in North America or in Europe, the lack of clear protocols for DNA banking may heighten the potential for future misunderstandings with depositors or for unforeseen legal liability. The dangers of DNA sample misuse or third-party access to information are real and likely to increase as more disease genes are isolated. A change in the regulatory framework governing genetic testing could influence the attitudes and help modify the practices of DNA bankers. Pressures for a wider commercialization of genetic testing could increase from private companies. There is a reasonable enough expectation of growth in DNA banking to justify setting up mechanisms to protect users as well as donors. The growing recognition of the banks' existence and a keener understanding of the need for DNA banking by diverse stakeholders will challenge and ultimately transform the social perception of human genetic research.