

Bartha Knoppers
American Society of Law Medicine & Ethics
DNA Fingerprinting and Civil Liberties Project
RO1-HGH002836-02
Workshop 3 Presentation
May 3, 2005

Introduction: Bartha Knoppers obtained law degrees from McGill and the University of Cambridge, as well as a doctorate from La Sorbonne. She currently holds the Canada Research Chair of Law and Medicine and chairs the International Ethics Committee of the Human Genome Organization. She is also a member of the Board of Genome. She's an expert in this field. She was a good friend of Dorothy Wertz and has been a good friend to the American Society of Law Medicine and Ethics throughout this entire project.

Bartha Knoppers: Good morning everyone. Even while we were waiting to know if this project was to be funded or not, Dorothy, Howard and I began working on this particular issue that has yet to be covered in any literature.

If Dorothy had lived to write it with Howard and myself, I'm sure there would be a more sociological aspect that she brought to all of her work with international comparisons. As you know, she was the only one who had the courage, along with John Fletcher, to write two books on the ethical and social issues of genetics - the first one covering eighteen countries and the second covering thirty five. I don't think we'll ever see anyone with that vision or courage again.

What I have tried to do is to look at this particular issue by using a sort of de facto and, I believe, diverse bank of these collections which arise out of tragedies. Should we, or could we even, contemplate further research uses from these samples collected under very tragic circumstances?

To answer that question, I first looked at what generally can be done with samples whether they are medical samples from routine work, samples that have been used for medical diagnosis, or those collected for a specific research project that someone would like to use for other research.

Second, I looked at what I think is a more pertinent class of ethical norms, strictly sticking to ethical norms here, except for countries, such as France, that have codified them. I have looked at deceased individuals who can no longer give their consent. As you know in such a collection there are both samples of the deceased victim as well as samples from family members given during these tragic circumstances for identification purposes.

And I also added – and I think this was brought up I think by Hank yesterday— what about research involving samples already collected from vulnerable individuals, however defined, usually children and incompetent adults. I've come

to some conclusions which I haven't checked with Howard yet, so I don't think I should talk about these issues today.

If you look at the history of the samples and biobanking, you can divide them into four different periods:

The first is what I call the re-implication of the samples, body tissues, etcetera from the time that the state gets them for biology and anatomy. That pretty well governed how body parts, if you like, were treated, other than the crime for grave robbing, until the notion of blood donation and organ transplantation. I started bringing the notion of 'the gift' into the area of samples and body parts as well as whole bodies for anatomy. Following the Nuremberg Code in 1947, we see the whole area of research on body parts and body samples colored by the horrific period of Nazi experimentation.

Yesterday, Arthur brought up the issue: could there be a duty to participate in research? *The American Journal of Bioethics* had a lead article in its latest issue in which someone dared to bring up this concept. Of the twenty commentaries, only one agrees with the author, Rosamond Rhodes. The commentary argues that we consistently in our Institutional Review Boards uphold the concept that research is wrong and, moreover, potentially evil, that we must protect the subject from research. Rather, we should say that research is a necessary and a social good that must be framed as responsible in terms of what people can and cannot do, and in particular, who will protect those who cannot protect themselves. At the same time, we must not alienate these vulnerable people; we must not put them outside the range of research that would be helpful to them.

So the re-implication framework followed Nuremberg until about 1990, when an article that I wrote in 1989 argued that DNA sampling should be considered a medical act. But you have to have some sort of framing for it. Why not deem them obligations of professionals such as physicians? And that's where it stayed until the article by Ellen Right in 1995, which was mentioned by Hank yesterday.

I wrote a follow up article to Right's article which I thought was unnecessarily conservative, entitled, "DNA Samples: Persons as sources, samples as persons" in *JAMA* in the same year, 1995. If you read that article you will see that the samples have become capitalized, that is, they have a life of their own. They're almost persons, samples as persons. But nowhere does the article talk about people, consistently throughout it talks about 'sources of DNA.' I found that contrast quite interesting. The friendly debate lasted until about 2000.

Now what we've hit is the third period, which I call bureaucratization, where there are now multiple, and contradictory, levels of review. We have examples of this around the world. But we now have bureaucratized ethics to the point where IRBs are quasi-judicial tribunals with no review and actually terrorize, in some

sense, a lot of researchers. The lawyers or jurists who sit on these IRBs are told that ethics is above the law.

My hope is that we can hit the fourth level, what I call internationalization. We can move to this fourth period where the nature of these tragedies and the nature of research itself are necessarily international. If we really are talking about the human genome at the level of a species, or genes in the level of persons or families and so on, we have to go beyond the individual, beyond re-implication and capitalization, and certainly beyond bureaucratization.

Now there's only one act that's really in the bill written by George Annas, as most of you know, that actually talks about use of samples from deceased following their necessary identification. That's in the Genetic Privacy Act, which simply says, "No. You cannot use them of research afterwards." In one of the excellent background papers it notes that the property approach and the ownership approach have been adopted only in four American states. And that kind of descriptive approach would necessarily limit any research uses of samples. After seeing that there is very little specifically on this subject, we will look at the norms in secondary use.

I have a recent project that is currently under review in which I found thirty-seven different ways to describe the identifiability of a sample. For simplification and for my purposes I just talk about anonymized strips of identifiers, those which are no longer identifiable, and as you know go through coding, either single or double. There is a big discussion whether people who receive double-coded samples are actually receiving anonymous samples.

So these are general principles that I think everyone in this room is aware of, that apply generally to samples. The principles, the need for consent, are generally found across clinical and research settings.

But this is interesting - and I am trying to illustrate this in particular examples –as of 2004 you can see a real move, even in countries that hitherto have been extremely restrictive and conservative in their approaches, such as Germany and France, with respect to secondary use of samples, in going back and recontacting, reconsenting and so on. Some exceptions are now appearing, as are more-nuanced approaches. People will, in their propositions, distinguish between degrees of identifiability and degrees of IRB oversight, a waiver and the like.

So a general overview of the text before we look at some specific ones is in order. I don't have to tell anyone here about the federal regulations, but generally if you are looking for waiver, anonymized samples do not constitute research on human subjects. In fact most countries do not take this position that anonymized samples are not considered research on human subjects. France falls into this category.

Up until August 2004, France required a new consent written for every further research use. As of August 2004 it has adopted a notification approach and no objection from an IRB review. The general waiver of consent requirements across different countries, which you will see, use the criteria of reasonability, limited risk, minimal risk, no objection, and the lowest level of identifiability of the samples necessary in order to do research. Not so strict that the data set is worthless, in other words. And this unfortunately has not been sufficiently explained, even in explanatory documents you do not find good examples of compelling reasons why you need them, which means you can go around all of these. For public emergencies other than a reference to SARS, there is nothing to do with bio-medical or identification research. Again this has been criticized. In August 2004 the Office for Human Research Protections actually took a very progressive position: if you have samples collected for one purpose and you want to use it for another, and if they are double coded and the secondary researcher does not have access to the key, then it's considered to be anonymized for those purposes and no recontact is necessary.

Another approach across the European Society of Human Genetics is to have consent requirements waived by an REB if the collection had been abandoned or the genetic material would otherwise be considered waste. This is now known as the Human Tissue Act, though the regulations for this act have not yet been released—the UK does not explain to you a very complicated act. It was written in reaction to the Alder Hey scandal, when children's organs were used for research without parental consent or knowledge, and it's been an imbroglio in terms of trying to understand the law, because we're waiting for the regulations to tell us what the law is saying. I can't tell you what it means.

In Germany's National Ethics Commission, if the research is of such importance that it outweighs the donor's interest, it would be disproportionate to ask for specific consent. Germany has a very good guide of protection. There is always the other side of the consent. You lower the criteria for consent but you up the level of data protection. They have data stewards and excellent data protection legislation. They also have the governing bodies to make this possible, like the National Privacy of Data Commission.

Let's turn now to deceased individuals. Is there anything? No, there is not much. There are the usual articles on autopsies and so on following suspicious deaths and that kind of thing in civil codes and laws around the world. But as we know from organ donation, the act of being deceased does not distinguish your interest in what happens to your body or leftover samples. And absent of known wishes, unfettered, uncontrolled use of samples from a deceased person and others are generally still considered to be unethical.

But that said, let's take another look at this blanket of ethics. Let's start nuancing what can or can not be done, because they haven't gone through this much.

I mentioned the Privacy Act, and other similar acts which talk about samples.

So now let's look at vulnerable individuals for a minute, which are children and incompetent adults. And as you know there is a much higher level of scrutiny and restriction in terms of their participation in research. Before Helsinki, from the time of Nuremberg, as you know, there was very limited research. And Helsinki opened it up to the benefit of that child, or children of the same age or similar conditions, making incompetent adults and children part of the general category, so they would not be completely excluded from research. But it's still quite restrictive. If you can't meet those particular criteria you cannot include samples from children or incompetent adults for research.

Then we also have the idea of trying to obtain their assent. They cannot legally consent, but you have to have at least some communication to know that there's assent. And then the REB obviously can also go through these criteria and limit them. Can the research be done with competent individuals, rather than do research with children or incompetents? Will the research benefit that individual or the category? Are the risks minimal, and so on. These are well known criteria.

You also have what we call de facto incompetence. Everyone is presumed competent until demonstrated to be otherwise. But you often have competent individuals who find themselves in emergency situations, such as shock or accidents or cerebral injury, and cannot be judged competent – usually in these situations, we transfer legal rights to the family members, because they fall under the context of care, as opposed to research. I don't want to get into a whole complicated area, but in some countries, the legal members who can consent for research are not the same as the family members who can consent for medical care. There are special rules for emergencies; put it that way.

Believe it or not, Germany is actually questioning these limits on quote, "children and incompetent adults in research," debating whether the very restrictive, minimum risk research cannot be done on other groups, unless there is a direct benefit to children in the study, and so on.

We have some new approaches, one being 'notification.' There's no objection of family members, believe it or not. "Appropriate consent" is another, though we don't know what that means because we're waiting for the regulations, and "no indication of objection from the family members" in Germany is a third new approach.

So I'd like to conclude on this part, and from here go on to mass disasters. We really see for the first time, an opening up in terms of secondary usage, though I'm not saying it's an open field. Very few countries have taken the position that deceased individuals or anonymized samples are not human subjects. This is

unique to the United States, but you can see it opening up both internationally and in particular countries.

So what do we do with all of this then, if we're looking at specificity at mass disasters? Well, obviously no one has really, other than in a terrorist situation, chosen to be in that situation. I'm not saying you've chosen just to be ill either, but you do have some control over your tissues and body parts. And family members who are called up to contribute are not exactly in an un-coerced situation. So you are dealing with a highly vulnerable group of people, either those who are deceased unwillingly or those who contribute samples as family members, who are obviously in a situation where waiver of consent should be an exception. In a tragedy, you don't go around with papers with lines on them and things to sign at the bottom and so on. It's completely out of the whole research hierarchy. But in any event we have to keep in mind that it is exceptional that we don't have written consent.

Can you then go back to these living family members later and ask them for further use? If you can't ask them right away, can you ask them later? That is the question. Obviously the answer is if there are living family members, then we should go back to them for consent.

In most cases privacy and confidentiality is already breached. They're contacted, they're brought in, and they're asked to be involved, but it's not a voluntary situation. They're known in their local community as having been part of that particular victimized situation.

Very little has been done on this – I went into the literature a little bit, but as I said in the absence of Dorothy, it's not exactly my forte to look at the reactions of trauma victims and psychosocial shock victims and so on. Can we start training from experience how the public would view, and how family members would view secondary uses of mass disaster samples? This is Dorothy's area of expertise.

So here are the possible approaches: following the French model, which doesn't address mass disasters, can you notify and see if either the public in general or the family members specifically come forward and agree to further use?

In principle, then, if you need written consent of the adequately informed, if the family member has not yet been identified, you're still looking. You're still coding, then you would need an informed written consent in order to maintain public trust in the entities, the police and forensic investigators to be trusted. I think you would have to follow a written consent for those samples that are still coded because you haven't found the individuals. REB approval is necessary, and you would have to make sure you have proper security and confidentiality counseling mechanisms in place.

Now, on to exceptions; first, research on anonymized samples could be permissible with REB review, if that research was to improve the identification with that particular disaster or a future disaster, then that would presumably be in line with what the victims or the families would have wished. To bring in the vulnerability part, as in children, if it's research that would benefit the class to which the individuals belong, linked with particular situations, not a disease, but the situations of mass disaster, then research may be feasible. And then there would have to be all kinds of security and so on.

In all respect to the victims of mass disasters and so on, you don't want to do like we did for years with pregnant women and children and incompetent adults, and say 'don't touch.' Let's be realistic; let's be principled and pragmatic at the same time. But limit research.