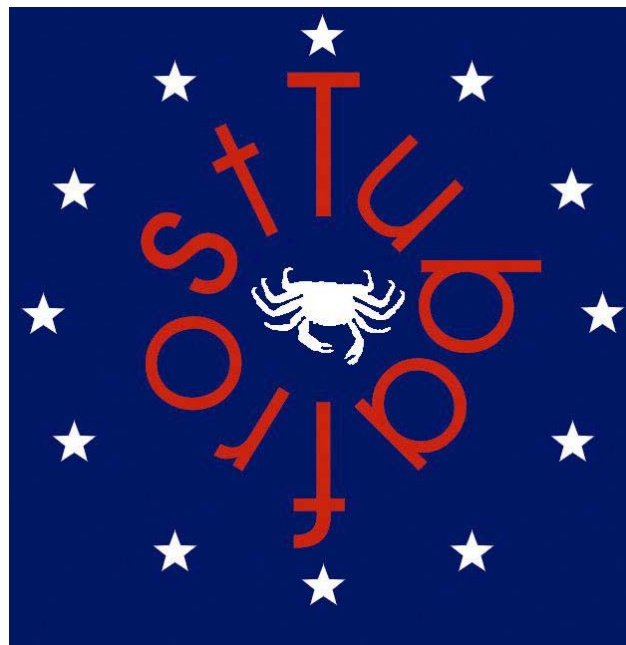


Quality of Life and Management of Living Resources  
**European Human Frozen Tumour Tissue Bank**  
**TUBAFROST**  
QLRI-CT-2002-01551

**Deliverable D 7.1**

**ETHICAL and LEGAL ASPECTS**



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## CHAPTER 1 INTRODUCTION

**1. Purpose and limits of this deliverable***1.1 Purpose*

This deliverable fulfils the aims of WP 3.1 of the European Human Frozen Tumour Tissue Bank project (TuBaFrost). In order to make tissue in various countries accessible for researchers in other countries, all parties need to know what rules apply to them in that context. Therefore a kind of 'reference book' is necessary with an overview for each country of the participating centres of relevant legislation and guidelines applicable in that country. This deliverable hopes to achieve that.

*1.2 Type of regulations to be addressed*

Many regulations might apply to researchers in a specific country. A laboratory might need a permission from a governmental agency to work with human tissue, there might be safety regulations to protect public health or the health of the employees or both, etc. We cannot address all these regulations. The regulations, guidelines and authoritative statements we are concerned with are those which directly relate to research with left over tissue<sup>1</sup>. Two types of regulations<sup>2</sup> are directly relevant in this respect:

- Those which describe which type of consent is needed for research with left-over tissue;
- Data protection and its application to research with or without genetic data.

The inherent limitation needs some clarification. We are not concerned with the informed consent process related to the procedure for removal of the tissue. It is obvious that in every country informed consent is needed for a medical intervention like this and we have to assume that that has been performed correctly by the treating physician according to the accepted patient rights of the country and the standards of the profession. The rules governing this process might become relevant though as from these also rules for consent to 'further use' might be derived.

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<sup>1</sup> Left over tissue means tissue which was taken out from a patient in the course of a diagnostic or therapeutic procedure and has been stored after it has been used for its original purpose (if there was any). Use of left over tissue for research or other purposes, like teaching or reference material, is named 'further use'. Use of left over tissue for quality assurance of the diagnostic process is not 'further use' by the way.

<sup>2</sup> We will speak of regulations here when we also mean 'guidelines' and authoritative statements from advisory bodies.

It is obvious that data protection regulation is relevant but data protection regulation is even more important than one might think at first hand. As yet there are in many countries no established regulations concerning 'further use'. As we will see, the topic is still 'under discussion'. Data protection legislation on the other hand provides, following EC Directive 95/46, relatively clear rules in each country. In the absence of clear regulations on 'further use' one must always fulfil the rules of data protection regulation as research with left over tissue always involves the use of data. The tissue is accompanied with at least some data about the 'source'<sup>3</sup>. Analysing the tissue for research will provide new data. These are also new data about the source even if the intention is not to reveal anything new about the source as such but about the type of tumour and, for example, its response to a given treatment. Of course, in the context of research the identity of subject should remain anonymous to the researcher but it is exactly the subject matter of data protection regulation under what circumstances anonymous but linked data may be processed (used and collected). Data protection regulation sometimes also holds rules about genetic data. The TubaFrost is neutral to the kind of research which will eventually make use of the TubaFrost tissue exchange program, but it is obvious that research in either the genetic properties of the tumour in relation to response to treatment or the genetic properties of the source in relation to tumour development (or to other variables) can be part of it. So special attention should be given to this subject as well.

### 1.3 *Limitations*

As said this Deliverable is meant as a reference for researchers who want to exchange tissue in the context of the TubaFrost resource.

However, it should be stressed that it can only serve as a *first* reference on the regulations for using left-over tissue for research in each of the countries. This for several reasons: The issue of research with left over tissue and tissue banking has not yet been explicitly addressed in the legal system of many countries, but this is rapidly changing. This deliverable describes our knowledge in a given moment of time, but might outdated when others read it. To take just one example, when finalising this report the UK Bill on human tissue appeared. We could add a brief and still superficial description of this important legislative proposal which would not have been possible if we would have delivered this report within the proposed schedule.

There is an ongoing discussion on the international level as well; the outcomes of this discussion and the available options will influence the application of national regulations even if these regulations themselves remain unchanged.

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<sup>3</sup> Hereinafter we will refer to the patient from whom the tissue was taken out as 'the source'. This is done by most writers on the subject.

As the law and ethical opinion is evolving, it is even hard to ascertain what the actual state of the law is at this moment in a certain country. Even legal scholars in that country might differ from opinion on certain aspects;

In general it is hard to know the state of the law in a certain country even in a field which is not as fluid as this one, when one has not the opportunity to study for some time in that country and discuss the issue with several key figures from various disciplines. In our survey (see the next paragraph) we have seen that ‘the state of the law’ as it was told to us by some lawyers of the country involved, can differ quite sharply from current practice and any more sophisticated legal opinion should accommodate for that difference.

Hence, this Deliverable has to be used with a certain care. We tried to be as accurate as possible, but there might be some deficiencies. Furthermore, even informed and reasonable lawyers of the country concerned might differ on opinion on the subjects we describe here. In an evolving field like this, much will depend on their starting point in the discussion. As will be described in more detail in section 3 of this and section 5 of the next chapter, we believe that a starting point which leaves as much room for research as can be justified, is both ethically and legally warranted. However, many legal scholars in this field start from the premise of – in short - as much patient rights as possible. From that perspective one arrives at different outcomes when the present unclear state of the law has to be articulated. The ‘*ius constituto*’ is often mixed with the ‘*ius constituendum*’ as these health lawyers would like to see it.

## **2. Method used for this Deliverable**

We gathered the material for this Deliverable in the following ways:

- literature;
- regulations of the countries concerned which we could find on the internet, we could buy here in the Netherlands or was sent to us by our respondents;
- The results of the questionnaire which we have sent to the participating institutions of the TubaFrost project<sup>4</sup>.

As this Deliverable is meant to be practical, we will only give references to the literature used if we clearly refer to a specific statement (either in agreement or in disagreement).

## **3. ‘Playing safe’ vs. opportunities for research**

### **3.1 ‘Playing safe’**

Our problem might have been avoided by ‘playing safe’, i.e. interpreting the regulations of each country in the strictest way. The most strict way would mean explicit consent for each research protocol for research with left over tissue and the necessity to (re)contact the

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<sup>4</sup> This questionnaire is added in appendix 1

patient concerned in order to ask permission if that had not been done previously. If the patient cannot be reached, then research will not be possible.

Research according to these lines of consent will nearly always be allowed but rarely be possible.

### *3.2 Opportunities for research*

However, apart from being an inaccurate description of the state of the law in many countries, such an approach would greatly undermine the value of this deliverable for the TuBaFrost project and comparable 'tissue banking' projects. We are foremost looking for legitimate opportunities for research, not impediments, though of course we cannot ignore those either.

Opportunities for research means that we have tried to describe the state of law as accurately as possible but also indicated where the discussion leaves room for interpretation which is more favourable for research than the stricter views. This follows from our personal convictions as well, as we feel that the legal and ethical discussion on research with left over tissue has focussed too much on patient autonomy and unwarranted analogies with research with human subjects. We will come back to that in the next chapter.

## **4. The 'cross border' aspect of tissue for research**

When, like with the TuBaFrost project, left over tissue may be used for research in another country (country of research) then where it has become available in the course of patient treatment (country of origin), two types of regulation may apply: that of the country of research and that of the country of origin as each country may have its own rules for the use of left over tissue for research.

If the country of origin has stricter rules than that of the country of research, the former may forbid the 'export' of tissue for research to latter country. If, on the other hand, the country of research has stricter rules, it may ban the use for research of tissue coming from countries with a less strict regime. We will address that problem briefly in section 5 of the next chapter of this Deliverable. The problem lies at the basis of Deliverable 7.2, for which the work on this Deliverable forms the start.

## **5. Set up of Deliverable**

As said the current state of the law in the various countries is influenced by the ongoing discussion on the international level, both in the international literature as in international organisations. A description of that discussion should come first and therefore has got a place in the next chapter. After that, the state of the law, as far as we can see it, will be described in each country, alphabetically ordered.



## CHAPTER 2 THE INTERNATIONAL DISCUSSION

**1. Introduction**

In this chapter we will discuss the main issues of use of left over tissue for research in the general literature (or 'further use' of left over tissue in general) and in some documents of national advisory bodies or international organisations. This overview cannot be exhaustive, as that would require a whole volume<sup>5</sup>. The idea is to give a description of the relevant topics and trends which can serve as a reference for the description of the national regulations. At the same time we would like to use the opportunity to give a critical appraisal of the current discussion. That will be done in the last paragraph of this chapter. First we will give a clarification of the relevant distinctions and of the terminology to be used. Then we will discuss the literature where we will take some documents of advisory boards into account as well. After that we will turn to the as yet few authoritative statements of international bodies, before - as mentioned in the previous chapter - giving our own critical appraisal of the discussion.

**2. Relevant distinctions***2.1 Relation with patient data*

As said, research with tissue is research with data as well. This is not to argue that research with tissue does not pose several questions which are distinct from research with 'just' medical data.

Obviously research with tissue does so because of the sensitive character of human material and the possible greater impact of research with tissue for the sources. But first of all, the conditions for research with data are more clearly defined in many legal systems. In the second place, the possible impact of the results of this research will depend on how the tissue can be linked to his identity. In the third place, and related to the former point, most discussions and reports on research with tissue make somehow a distinction between types of tissue which is based upon the classification of the accompanying data: how the source's

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<sup>5</sup> and those exist already, see P. Weir, stored tissue samples: ethical, legal and public policy implications, University of Iowa Press, 1998, M.G. Hansson (ed), The use of human biobanks, ethical, social, economical and legal aspects. Uppsala, Universitetsstryckeriet, 2001 (which describes the ongoing research in this subject); C. Trouet, Van lichaam naar lichaamsmateriaal, Recht en nader gebruik van cellen en weefsels, Intersentia, 2003; M.G. Hansson, M. Levin (eds.), Biobanks as resources for health, Uppsala, Universitetsstryckeriet: 2003. Furthermore various reports from advisory bodies some of which will be discussed later in the text.

identity can be linked is of paramount interest for the type of consent (see the next section).

In that respect the following distinctions can be made:

(directly) identifiable tissue: data accompanying the tissue are such that the researcher knows or can know without employing excessive means the identity of the source;

linked or coded tissue: the identity of the source remains unknown to the researcher but the identity can be retrieved by the provider of the tissue, like the source's treating physician by a code which has been added to the tissue<sup>6</sup>;

Fully anonymous tissue: the identity of the source can not be retrieved without employing excessive means.

These three types are always distinguished, but often under other names. Above terms seem to be the most common denominators. Some publications also mention the relevance in the third category of the question whether the tissue – and so outcomes of research – can be linked to a certain minority group. In that case 'group privacy' might be at stake.

The term 'without employing excessive means' is rarely used in the discussion in most reports. It stems from the European privacy debate, where its positive counterpart has been incorporated in the European Union Data Protection Directive to discern identifiable from not identifiable or anonymous data: 'by means likely reasonably to be used' to identify the data subject. This helps us to add some common sense to the notion of identifiable. Not everything which could be done in theory to identify someone, is likely reasonably be done under the given circumstances: this controller and the means he has available and is likely to employ.

The second category poses the question whether coding is just a precautionary procedure to safeguard the privacy of the source or that it should lead to a different treatment of the consent question as well. Before addressing that question it should be stressed that the answer is not clear for research with just data either, or more precisely, the classification of the middle group 'coded data' is not clear in relation to the EC data protection Directive which only knows two categories: identifiable and anonymous data. In some countries, like Belgium, (two way) coded data are considered identifiable data. In other, like the Netherlands, these data are considered to be anonymous. The evaluation of the Commission of the Data protection Directive and the underlying report did not choose between one of the two options<sup>7</sup>.

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<sup>6</sup> Technically speaking we are dealing with two way coded tissue. With two way coded tissue there exist two keys for the coding system: one for the identifiable data of the patient to the unique code number and another key for the unique code number back to the patient's identity. With one way coding only the first type of key exists. It should be stressed that in both cases the researcher has no key whatsoever. He gets the coded material, but cannot generate the code number, let alone decode the number to the patient's identity.

<sup>7</sup> More on this evaluation and these distinctions in E.B. van Veen, *Gecodeerde data en wetenschappelijk onderzoek*, Privacy & Informatie, December 2003, in print.

It should be noted, however, that in the discussion in the US literature and documents based on the US discussion<sup>8</sup> (two way) linked or coded data are considered 'identifiable'. With respect to tissue research there is another aspect to the discussion which influences the classification. Linked tissue would in theory create the possibility that the results of the research can be communicated on an individual level to the source (via the treating physician, as the identity will remain unknown to the researcher). Therefore, the impact of research with linked or coded tissue could be the same as with directly identifiable tissue. Possible feed back merits separate attention. We will come back to it in section.... of this chapter. It should be noted here that this question does not arise if the data accompanying the tissue were only 'one way' coded. The distinction between one and two way coding (see note6) is rarely made in the literature, but is of paramount importance. With one way coding the issue of 'feed-back' does not play a role at all as such feed back is impossible. One way coded should be considered to be anonymous; whatever position one holds about two way coded data.

The last point of discussion of tissue research in relation to the data protection terminology is whether tissue can ever be anonymous. There are some statements which argue that because of DNA mapping tissue can in most cases be linked to the individual source<sup>9</sup>. To us this seems a gross exaggeration of the possibilities of DNA mapping and an undervaluation of the technical and procedural safeguards which should govern a research establishment. Even if a DNA profile would be drawn from the tissue, this profile could only reveal the identity of the source if this could be matched with an already existing profile with the source's identity linked to it. Such profiles might exist at certain forensic centres but researchers do have access to them and have not tried to get access to them either<sup>10</sup>. If this line of reasoning would be used for long time existing techniques then it could be argued that nobody can visit a hospital anonymously when having a cup of coffee or glass of water there as his fingerprints might be matched with those in the files of forensic centres. A slightly more plausible argument would be that DNA mapping might be performed on the anonymous tissue in the research facility of the health care centre and on identifiable tissue at the treatment facilities of the centre and then the two sets might be matched. This is a theoretical possibility, which anyhow does not hold true if tissue is exchanged between

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<sup>8</sup> as, as it seems, in the revised Declaration of Helsinki (Edinburgh, 2000) of the World Medical Association.

<sup>9</sup> Medical research Council of Canada, Natural Sciences and Engineering Research Council of Canada, Social Sciences and Humanities Research Council of Canada, Tri Council Policy Statement, Ethical Conduct for Research involving human subjects, especially section 10, 1998, as revised in 2000, see <http://www.nserc.ca/programs/ethics/english/policy.htm#contents>. Hereinafter referred to as the Tri Council Statement.

<sup>10</sup> it might be tried the other way around, this is a separate discussion which will not be addressed here.

centres and the donor in all likelihood will never have visited the receiving centre. And even in the case where the tissue remains in one centre, it should be emphasized that both research and clinical analyses of the tissue is done under strict standards of supervision and will have to stick to the protocol describing the question to be answered. Any other procedure would be illegal and could never be performed on a scale large enough to achieve the 'desired' result. Desired between quotation marks as there are no known cases where researchers have been that eager to retrieve the identity of the donor.

## 2.2 Variations in consent for research

The discussion on 'further use' of tissue centres on the question of consent. The question is not as much whether consent should be given but how and what kind of consent. As the consent paradigm for 'further use' - though accepted at this moment - is relatively new, there is also the question of what to do with existing tissue repositories where it is unclear that the donor has given consent to 'further use'.

In theory several types of consent can be distinguished, as shown in the following scheme (scheme 1).

.....	identifiable (a)	linked (b)	anonymous (c)
explicit consent for each specific protocol (research question)			
explicit consent for a specific type of research (like cancer research)			
explicit consent for research in general (blanket consent)			
as 2 but with additional specific consent (or not) for genetic research			
as 3 but with additional specific consent (or not) for genetic research			
consent is presumed but opt out possibility			
No consent, research may be performed			
use of an existing repository			

We have left the option, sometimes seen in the US literature that the donor should also have a say whether tissue may anonymized. Once it is, it may be used for research without a specific consent procedure.

Option one for tissue type a and b can be seen as the most strict form. Option 2 for a and b is rarely used alone. Usually we see a type of 'layered consent' like 4 with the addition of 3 as the last option. Blanket consent is seen by many as no consent at all but in addition with more strict possibilities from which the source may choose, it may be offered according to these authors<sup>11</sup>.

We do not take a stand on the issue of consent yet. Suffices to note that many variances are possible.

These variances become even larger if the issue of possible feed back is taken into account. Individual feed back may be given as a choice or not. In some studies individual feed back is foreclosed<sup>12</sup>. In that case a subject can not enter the study if he or she insists on individual feed back.

With respect to existing repositories, where no consent was given for research (or it is unclear whether consent had been given) the following options are in theory available:

- consent (of one of the type between 1 to 4 of scheme 1) should be sought retroactively from the sources. If the sources cannot be retrieved or if they do not consent research is not possible;
- consent (of one of the type between 1 to 4 of scheme 1) should be sought retroactively from the sources or, when they have died, from their relatives. If the sources or their relatives cannot be retrieved or if they do not consent research is not possible;
- consent (of one of the types between 1 to 4 of scheme 1) should be sought retroactively from the sources or, when they have died, from their relatives. If the sources or their relatives do not consent, research is not possible. For those who do consent obviously research may be performed. But if they cannot be retrieved after sincerely trying so, the research may also be performed on that tissue.
- The sources are made aware of the possible research via advertisements in the media and are given the possibility to opt out. Research is possible on the samples of donors who do not react.
- Research is possible when the research has possible benefits for health care or specific groups of patients and possible negative effects for the donors are considered to be non existent or minimal.
- Research is possible when the research has possible benefits for health care or specific groups of patients which outweigh the possible negative effects for the donors.

A combination of some of the options is of course possible as well.

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<sup>11</sup> Like Trouet, o.c..

<sup>12</sup> Like the UK biobank study. This study does not involve 'further use' but the rationale for not giving individual feed back can be the same in studies which make use of already existing material.

### 2.3 *The source is not a research subject*

In the discussion in the US the existing regulations on research with human subjects are applied to research with left over tissue and the person who's tissue is being used is seen as 'research subject'<sup>13</sup>. In the European discussion this rarely the case and quite rightly so. Research with left over tissue has a completely different impact on the person concerned than a trial where the person is subjected to a specific treatment regime<sup>14</sup>. Therefore we will use the word source, even though to some that might be depreciation of the dignity of the person concerned. The word donor is less suited, as this would easily mix the issue with that of organ donation and furthermore, in many cases there will not have been an explicit act of donation.

## 3. The interests which are at stake

### 3.1 *Balancing interests on the side of the source against that of (possible results of) research*

As with all ethical and legal discussions, it necessary to discern the different values or interests at stake and to balance them if they do not point in the same direction.

We would distinguish the following at the side of the sources or their near relatives

- autonomy of the subject;
- privacy protection;
- protection from harm.

We will discuss these further in section 3,3 first we will have a look at the interests attached to research.

### 3.2 *Interests at the side of research*

At the research side, we do not see interests attached to individuals but to a societal goal, namely medical research. Medical research, when looking at it more closely, stands for many interests. It might further economic growth, it is an expression of freedom of thought and expression, it furthers our understanding of ourselves as vulnerable living beings and can offer knowledge to prevent disease or offer a better treatment. These are very different interests, which must be weighed differently. We would like underscore that last mentioned interest means that at the side of research also prevention of harm is involved, though the individuals who will be protected can in most cases not be nominated yet. Therefore not

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<sup>13</sup> see e.g. the National Biotechics Advisory Commission, Research involving human biological materials: ethical issues and policy guidance, Vol I, Rockville, Maryland: National Bioethics Advisory Commission, August 1999.

<sup>14</sup> See also B.M. Knoppers, C.M. Laberge, Research and stored tissues,. Persons as sources, samples as sources, JAMA, 1995, p. 1806-1807; D. Wendler, What research with stored samples teaches about research with humans, Bioethics 16, 33 (2002).

only interests of society at large are involved in research, as is mentioned in all publications, but those of very specific groups at risk, even though the individuals concerned can in most cases not be identified yet and it also uncertain whether research will be able to ward of these risks in the near future.

This is an important contention, as it underscores two points. First that also in tissue research one can speak of concrete potential benefits, like in medical trials, though unlike trials the benefits usually do not fall to the participants. Secondly that the juxtaposition of interests of the source on one side and of research on the other side is not one of, paraphrasing Dworkin<sup>15</sup>, 'personal rights as trumps over societal goals', as it is commonly understood. The relationship is far more complex and any balancing of interests should take these complexities into account. We will come back to that in the last section of this chapter.

This is not meant to say that of course that the 'considerations related to the well being of the human subject' should not take precedence 'over the interests of science'. This principle of the Helsinki Declaration (14, Principle A.5) should always be followed. In the following section we will discuss how the well being of the subject can be involved in tissue research.

### 3.3 *A closer look at the interests of the subject*

- autonomy

Autonomy is deeply rooted in the value system of the modern Western world. It is closely connected to the principle of respect for persons. Together with a growing emancipation of the public autonomy got ramifications which it did not had before. Originally the destination of left over tissue was not seen as falling within its ambit. This changed in late eighties of last century due to the growing recognition of patient rights and growing concerns about the possibilities of research. By now all it is assumed that the patient should be able to decide upon possible special 'further use' of left over tissue under most circumstances.

- privacy

As we have seen, tissue research is to a large extent also research with data. Research on tissue reveals data about the source and usually tissue is accompanied by such data. In a later stage these data might be compared with follow up data of the source from his medical record or other data-sources.

So we obviously have a privacy issue here. This privacy issue works two ways. First privacy protection is needed in the process from collecting tissue and making it available for research and within the research project: collecting only these data which are strictly necessary for a given research protocol, access only by authorized persons, separation between datasets held for care and datasets held for research, etc.<sup>16</sup> and privacy enhancing

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15 R. Dworkin, *Taking rights seriously*, Duckworth, London, 1977.

16 these measures are described in detail in the Dutch Code Proper Use, Code for research on tissue by the Federation of Medical\_Research Associations, 2001, see [www.fmwv.nl](http://www.fmwv.nl)

techniques for possible necessary linking of research data with clinical data.<sup>17</sup> Second, the data following from the research on the tissue concerning individuals might be used against them if they came in the hands of third parties. That would or could result in harm, so we will discuss that below.

– harm

Harm can arise in many ways. Unlike medical trials, physical harm for the subject is not possible when his or her tissue is used in research, but other types of harm are feasible. psychological harm when research is carried out without consent

Some publications reports mention 'psychological harm' which people might feel if they became aware that their tissue is or was used in research without their consent or even knowledge.<sup>18</sup>

results used against the subject caused by a breach of confidentiality

More tangible is the harm which might accrue if their data come to be known outside health care. This is a point of serious concern in most publications. Individual data following from research could get to be known by third parties in two ways. First they might be collected by third parties directly from the researcher or the research institution. This would mean that the data have been used contrary to their original intention. Either the researcher must have breached his obligation of medical confidentiality or the third party must have deliberately broken in the system of the researcher or the institution in which case this party has committed an illegal act as well by breaking into a secured system while the safeguards of the researcher (or the institution) have been insufficient.

Neither has, as far as known, ever happened and both seem extremely unlikely scenario's. The research community may have found difficulties in accommodating to new views on as it called by some German authors 'informational self-determination' but has a long and unchallenged tradition of protection privacy of subjects towards third parties. Third parties, like insurers, can have an interest in knowing the (future) health status of an applicant, but that they will hack in a computer system of a research institution where they suspect that the applicant will be stored as a subject, is to our opinion an unfeasible scenario. However, in

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<sup>17</sup> Medical Research Council, Human tissue and biological samples of use in research, Medical Research Council: London 2001, see [www.mrc.ac.uk](http://www.mrc.ac.uk). Hereinafter referred at as the MRC report; Ashburn TT, Wilson SK, Eisenstein BI, Human tissue research in the genomic era of medicine, Arch Intern Med. 2000; 160:3377-3384; European Society of Human Genetics, Data storage and DNA banking for biomedical research, draft valid until \* October 2001, section 18.

<sup>18</sup> Medical research Council of Canada, Natural Sciences and Engineering Research Council of Canada, Social Sciences and Humanities Research Council of Canada, Tri Council Policy Statement, Ethical Conduct for Research involving human subjects, especially section 10, 1998, as revised in 2000, see <http://www.nserc.ca/programs/ethics/english/policy.htm#contents>. Hereinafter referred at as the Tri Council Statement;



the US and Canada<sup>19</sup> it seems that subjects need to be warned in the informed consent procedure against this 'risk'.

The second possibility is that the subject him or herself reveals this information by accident or upon request. That presupposes that this information is known to him or her. We deal with that subject below and in section ...

harm from knowing the results of research applicable to the subject

In paragraph 4 we will discuss the problem whether and how subjects should be informed about the results of research applicable to them. When information is given, this can be reassuring but in many cases it is not. This is especially the case if these findings are of a genetic nature pointing at the probability or even certainty of developing a disease. Even if a treatment is available, this knowledge will put great strain on the individual, can effect his future life choices, including procreational choices, family relations and socio-economic status (see below). If no validated treatment is available, things will obviously become worse, in most cases to the point where the subject will think that he would have been better off if he or she had not consented to this tissue research.

This being said, such information will be extremely rare research with left over tissue and can be avoided in most other cases. The Report of the Medical Research Council<sup>20</sup> on tissue research quite correctly distinguishes between applying genetic tests of known clinical or predictive value and other tests. In general there can be no scientific reason to apply tests of the first kind on existing samples unless in the course of an epidemiological research in which case they usually could be fully anonymized.<sup>21</sup> The other reason for applying tests of known predictive value would be that other predictive values are thought than those known already, a new correlation between phenotype and genotype is thought. It takes a very long way of testing, validating and establishing its clinical relevance before the

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<sup>19</sup> Medical research Council of Canada, Natural Sciences and Engineering Research Council of Canada, Social Sciences and Humanities Research Council of Canada, Tri Council Policy Statement, Ethical Conduct for Research involving human subjects, especially section 10, 1998, as revised in 2000, see <http://www.nserc.ca/programs/ethics/english/policy.htm#contents>. Hereinafter referred at as the Tri Council Statement; NCI site and model consent; Deschenes M, Cardinal G, Knoppers BM, Glass KC, Human genetic research, DNA banking and consent: a question of 'form'? Clin Genet 2001; 59; 221-239

<sup>20</sup> Medical Research Council, Human tissue and biological samples of use in research, Medical Research Council: London 2001, see [www.mrc.ac.uk](http://www.mrc.ac.uk). Hereinafter referred at as the MRC report; Ashburn TT, Wilson SK, Eisenstein BI, Human tissue research in the genomic era of medicine, Arch Intern Med. 2000; 160:3377-3384; European Society of Human Genetics, Data storage and DNA banking for biomedical research, draft valid until \* October 2001, section 18.

<sup>21</sup> 'Population studies' will not be discussed here, they raise questions which are different from the type research based on 'further use' discussed in this report

results of this kind of research can be said to of such a nature that the subject has a right to informed about it (see section...).

Apart from that, the way these tests are performed are usually not according to clinical standards. In research it usually is sufficient to establish statistical links for which a margin of error of the tests is acceptable which would be unacceptable on the individual level. But feed back remains a concrete possibility in some cases and if feed back is foreseen, this should be discussed with the subject also because of its possible socio-economic consequences.

harm in the socio-economic sphere

The mere knowledge of having a disease or a probability to develop one, can lead to problems when applying for a job or an insurance. This is by no means new. Risk selection is as old as insurance. But genetic tests have added a new dimension to it. The risk for exclusion increases when occasions where people will be informed on probabilities to develop a disease increase, as can be the case when their tissue has been used in research. This is an obvious disadvantage which subjects should be informed about and should be able to consider. The disadvantage will be even greater in countries, like the US, where statutory insurance schemes for the whole population based on risk solidarity for major negative life events like serious illness or unemployment are nearly non existing. In European countries comparable problems arise for other insurances which are part of someone's financial planning.

However, one may wonder whether this is really a danger inherent of research with left over tissue. It can be easily be avoided by not giving feed back to the source, or by warning the source of this possibility if he or she insists on receiving feed-back. If the source then nevertheless insists on feed back the situation for the source will not be different from the situation where a clinical test is requested by the source on his own initiative.

Next to this, the possible socio-economic harm does not stem from the research as such, but from sometimes unbalanced societal structures and something should be done about that. In all countries initiatives can be seen to limit drastically the possibilities for insurers or employers to require a genetic test as condition for acceptance and some countries have adopted measures against 'discrimination' based on genetic profiles or other possible risk factors<sup>22</sup>.

#### **4. Feed back to the individual sources**

This issue has been touched upon already. Two sub questions can be discerned:

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<sup>22</sup> In general Ashburn TT, Wilson SK, Eisenstein BI, Human tissue research in the genomic era of medicine, Arch Intern Med. 2000; 160:3377-3384; specific examples see art. 67 of the Austrian Gentechnikgesetz, the Dutch Law on medical examinations, art. L. 1131-1 of the French Public Health Act. See also the recent opinion of the European Group on Ethics on ethical aspects of genetical testing in the workplace (no.18, July 2003).

- Should individual feed back always be offered as an option?
- When individual feed back is foreseen as an option, under what circumstances may it actually be given?

Is it mandatory to offer the option of individual feed-back?

The answer is a clear 'no', unless the treating physician is doing research with samples of some of his actual patients. Such a situation, where the research rarely ever can be performed on anonymous samples and usually not even on coded samples, is very different from the situation where samples are used, often years after treatment, in a separate research facility. In the case of the treating physician, it would be a breach of the trust between doctor and patient if the first would withhold information which may be relevant for the latter.

But in the standard situation things are very different. The reasons for not offering individual feed back are described in the Background Document for the UK biobank ethics and governance framework<sup>23</sup> (at section I.B.3.c). In short and paraphrasing: research is looking for general trends, not for predictions about individual sources; the time interval between the moment the tissue was taken and the research; the fact that, as already mentioned, other techniques are used to find statistical correlations than to find clinical data about a patient; the fact that clinical relevance and its appropriate application in health care<sup>24</sup> of research findings are seldom clear from the onset.

The argument that with feed-back researchers would have to become counsellors, seems less relevant to us. The findings could be communicated to the treating doctors or general practitioner of the source as anyhow the researcher will not even know the identity of the source.

We find another argument much more important. This argument seems somewhat overlooked in the discussion. That argument is that general results of research are applicable to each and everyone who share certain characteristics, found to be relevant in the research, not only to the sources whose samples have been used in order to arrive at these results. That is the very essence of scientific findings. So even if there would be a ready application in health care, this should reach the whole group of the population for whom this application is of importance, and all efforts should be geared towards that objective, not on retrieving the sources to communicate it just to them.

If individual feed-back is offered as an option, what are the conditions under which it may or must be given?

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<sup>23</sup> Version 1.0, September 2003.

<sup>24</sup> also related to the ethical aspects and the cost factor of introducing a new technique or treatment option in the clinic

First of all, if individual feed-back is an option, non-feed back should be an option to the source as well. He has the 'right not to know' and should be able to execute that right. The source should have the explicit possibility to choose for this option in the consent procedure<sup>25</sup>.

To those who have opted for individual feed back, such feed back of the results of research can only be given if these results are scientifically validated and have implications for the future health of the subject)<sup>26</sup>. The NBAC report (p. 72) adds two other requirements: these implications should be *significant* and a 'course of action to ameliorate or to treat the health risks should be readily available'. As we have seen many publications stress that a scientifically validated fact is not by itself a clinical fact. Before that point is reached usually further discussion must have taken place between scientists and clinicians and perhaps other disciplines like ethicists. Instances where feed back is appropriate will therefore be rare<sup>27</sup> and the source should not be misled into expectations about possible new information he might get.

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<sup>25</sup> In the Dutch Code on Proper Use this topic is treated as follows. As the regulation is based on opting out for the use of coded tissue for scientific research, no consent discussion will take place. In the general information which gives the patient (=potential source) the possibility to opt out, it is stressed that as a rule no individual feed-back will be given. If the source wants that, he has to opt in for that option. When opting in, a true consent discussion will take place whether feed back is really what the patient wants and in his best interests.

<sup>26</sup> National Bioethics Advisory Commission, Research involving human biological materials; ethical issues and political guidance, Vol. I Rockville, Maryland: NBAC, August 1999. see [www.bioethics.gov](http://www.bioethics.gov) Hereinafter referred to as the NBAC report ; Medical Research Council, Human tissue and biological samples of use in research, Medical Research Council: London 2001, see [www.mrc.ac.uk](http://www.mrc.ac.uk). Hereinafter referred at as the MRC report; Ashburn TT, Wilson SK, Eisenstein BI, Human tissue research in the genomic era of medicine, Arch Intern Med. 2000; 160:3377-3384; European Society of Human Genetics, Data storage and DNA banking for biomedical research, draft valid until \* October 2001, section 18.; these measures are described in detail in the Dutch Code Proper Use, Code for research on tissue by the Federation of Medical\_Research Associations, 2001, see [www.fmwv.nl](http://www.fmwv.nl); Deschenes M, Cardinal G, Knoppers BM, Glass KC, Human genetic research, DNA banking and consent: a question of 'form'? Clin Genet 2001; 59; 221-239

<sup>27</sup> Medical Research Council, Human tissue and biological samples of use in research, Medical Research Council: London 2001, see [www.mrc.ac.uk](http://www.mrc.ac.uk). Hereinafter referred at as the MRC report; Ashburn TT, Wilson SK, Eisenstein BI, Human tissue research in the genomic era of medicine, Arch Intern Med. 2000; 160:3377-3384; European Society of Human Genetics, Data storage and DNA banking for biomedical research, draft valid until \* October 2001, section 18; these measures are described in detail in the Dutch Code Proper Use, Code for research on tissue by the Federation of Medical\_Research Associations, 2001, see [www.fmwv.nl](http://www.fmwv.nl); Deschenes M, Cardinal G, Knoppers BM, Glass KC, Human genetic research, DNA banking and consent: a question of 'form'? Clin Genet 2001; 59; 221-239

The Dutch Code underscores that it should never be the researcher to give this feed back. Usually the subject will not be known to him anyhow. If any, feed back should be given by the (originally) treating physician and be embedded in appropriate counselling and referral procedures if the circumstances so require<sup>28</sup>.

### 5. Some responses by scientists: interests *and* values

In its statement on 'further use' The (UK) Royal College of Pathologists sighed that that 'autonomy' in the original Kantian meaning does not really seem to point at a position where you will profit from the results of research, but may at all points refuse to contribute even if there is no possible danger involved in such a contribution<sup>29</sup>. More recently the pathologist Furness repeated the importance of reciprocity involved in 'further use' and pleaded an opt out system for 'further use' as a sufficient guarantee for those who refuse to contribute without putting to much strain on the system<sup>30</sup>. His call caused a stream of approving reactions on the BMJ site<sup>31</sup>.

The Dutch Code on Proper Use proposes the opt out system for 'further use' on anonymous and anonymous but linked tissue. The Code was drafted in close cooperation with patient groups. These patient groups, however, were composed of chronically ill and cancer patients and not the casual visitors of the health care system. Also in England it seems that such patients have pleaded for less impediments for research on data and tissue<sup>32</sup>.

Apparently something more is at stake on the side of patients than arguments which would plead against 'further use' as mentioned in section 3.3. Patients who recognise their (or of those who will come after them) dependency on the possible results of research value this

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<sup>28</sup> Medical Research Council, Human tissue and biological samples of use in research, Medical Research Council: London 2001, see [www.mrc.ac.uk](http://www.mrc.ac.uk). Hereinafter referred to as the MRC report; Ashburn TT, Wilson SK, Eisenstein BI, Human tissue research in the genomic era of medicine, Arch Intern Med. 2000; 160:3377-3384; European Society of Human Genetics, Data storage and DNA banking for biomedical research, draft valid until \* October 2001, section 18; these measures are described in detail in the Dutch Code Proper Use, Code for research on tissue by the Federation of Medical\_Research Associations, 2001, see [www.fmwv.nl](http://www.fmwv.nl)

<sup>29</sup> Transitional guidelines to facilitate changes in procedures for handling 'surplus' and archival material from human biological samples, under the numbers 9-10. Found on <http://www.rcpath.org/prinfriendly.php?PageID=208>, last visited at 4-11-2003.

<sup>30</sup> P. Furness, Consent to using human tissue, implied consent should suffice, BMJ 2003, p. 759-760

<sup>31</sup> (<http://bmj.bmjournals.com/cgi/letters/327/7418/759>, last visited on 10-10-2003.

<sup>32</sup> See the example mentioned by H. Cayton, S. Denegri, Is what's mine my own?, Journal of Health Services Research, juli 2003, supplement 1, p. 33-35, op p. 34. These authors oppose by the way to become too lenient in admitting research. However, the conditions which are mentioned by them are quite reasonable and do not pose the real threats to data and tissue research which follow from some of the reports mentioned earlier in this chapter.

research more than the possible dangers of it, which indeed never have happened in reality either.

The issue wouldn't be so critical if the approach which follow from most in the reports mentioned in section 3.3 did not pose some real dangers to research. There are clear indications that a consent system for research on data or tissue can lead to a bias in the research<sup>33</sup>. In a letter in the BMJ it was reported that the recruiter of tissue for a commercial tissue bank get little refusals by taking about 15-30 minutes per patient<sup>34</sup>. Of course, such an investment would be impossible for non commercial research to which (amongst others) the partners of the ETB are committed.

Much more could be said about this topic, also on the so called 'right to self determination' which according some lawyers<sup>35</sup> should be the basis for an explicit consent system<sup>36</sup>, but this is not the place for such a full discussion.

The aim of this brief survey was to show that other relevant perspectives exist than those prevailing in most of the ethical and juridical literature. This is important as in the discussion on exchange of tissue for research between countries each country, at least of those who have considered the subject, seems require that his consent system should be followed. With organ donation every country has its own type of consent system, but this has not lead to a ban on the import or export of organs for patients on the waiting list in the other country. To our opinion this should not happen with the exchange of tissue as well. This will further elaborated in next years Deliverable 7.2.

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<sup>33</sup> V.C. Angus, V.A. Entwistle, M.J. Emslie, The requirement for prior consent to participate on survey response rates: a population based survey in Crampain, BMC Health services research, 2003, nov. 18 (abstract van Pubmed); J.A. Hoppin, P.E. Taylor, J.C. Schroeder, E.A. Holly, Potential for selection bias with tumour tissue retrieval in molecular epidemiology studies, Annals of Epidemiology, 2002, January, 1-6 (does not discuss bias by consent procedures but by lack of uniform information with the tissue, shows to my opinion how critical the availability of sufficient tissue is for this kind of research); S.H Woolf, S.F. Rothemich, R.E. Johnson, D.W. Marsland, Selection bias from requiring patients to give consent to examine data for health services research, Archives of Family Medicine, 2000, 1111-1118; S.J. Jacobsen, Z. Xia, M.E. Campion, et al., Potential effect of authorization bias on medical record research, Mayo Clinic Proceedings, 199, april, 330-338; P.A. Rumetti, R,G, Munger, J.C. Murray et al, The effect of follow-up on limiting non-participation bias in genetic epidemiologic investigations, European Journal of Epidemiology, 1998, 129-138.

<sup>34</sup> A.L. Jack, C. Womack, Why surgical patients do not donate tissue for commercial research: review of records, BMJ 2003, p. 262.

<sup>35</sup> E.g., Trouet, o.c.

<sup>36</sup> one may wonder what the self has to do with some deep frozen tissue which is anonymously studied.

## International instruments

### 1. Introduction

This paragraph can be very short when we only take the binding legal instruments into account. There are hardly any. There is somewhat more material in the field of data protection than in the field of 'further use' of human tissue. We will discuss both topics separately in the following sections. With regard to 'further use' we will mention some of the non binding instruments as well but will not try to be exhaustive.

### 2. Data protection

#### 2.1 *Recommendations of the Council of Europe*

Two Recommendations of the Committee of Ministers of the Council of Europe are relevant in this respect:

Recommendation No. R (97) 5 on the protection of medical data.

Recommendation No. R (97) 18 concerning the protection of personal data collected and processed for statistical purposes.

Although these recommendations are not binding, they are very influential and will for example play a role in the interpretation of art. 8 of the European Convention for the Protection of Human Rights and Fundamental Freedoms. Yet, both recommendations do not need to be discussed here. Their provisions are rather general. If applicable they will come into play when explaining the admissibility of a specific arrangement for processing data in the context of research within the room which is left by the EC Data Protection Directive in that respect.

#### 2.2 *The EC Directive on the protection of individuals with regard to the processing of personal data and the free movement of such data (95/46/EC)*

This Directive has been mentioned on several occasions already. As this Directive provides the European framework for the national data protection legislation and for the, allegedly, free flow of research data between the member states, it is of paramount importance. But also this Directive should not be discussed by itself, but in a given situation. We will come back to it in the country reports and the concluding chapter.

### 3. 'Further use' of human tissue

#### 3.1 *Non binding instruments*

There are several non binding declarations of international organisations in which 'tissue banking' of 'further use' of left over tissue is addressed<sup>37</sup>. We will not discuss all these but should briefly mention the revised Helsinki Declaration of the WMA. With the latest revision (2000, Edinburgh) article A.1 states "Medical research involving human subjects includes research on identifiable human material of on identifiable data". The influence of the American doctrine is obvious here. It is unclear how this definition relates to the other provisions of the Declaration which are clearly aimed at clinical trials and other comparable research to which subjects have to actively participate.

The 'European group on ethics in science and new technologies' issued a statement on the ethical aspects of tissuebanking in 1998<sup>38</sup>. The statement is most of all concerned with the use of tissuebanks for the preparation of allografts. That aspect is not relevant here. About the consent issue the Opinion is rather vague. Of course, informed consent is needed for the removal of tissue, but it leaves it to member states to determine the type of consent for 'further use', which also may 'presumed'.

#### 3.2 *Binding instruments*

##### 3.2.1 The Biomedicine Convention

There is as yet only one, namely the Convention on Human Rights and Biomedicine of the Council of Europe (Orviedo, 04.IV, 1997). Art. 22 of the Convention states:

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.

The explanatory report stresses the flexibility which this provision allows. In some cases it will be sufficient that a patient or his representative has not expressed opposition, in other cases express and specific consent will be necessary, in particular where sensitive information is collected about identifiable individuals.

Little is left of this flexibility in the proposed protocol to the Convention on the use of archived human biological material for research<sup>39</sup>. As this proposal might be changed considerably, it will not be discussed here.

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<sup>37</sup> Like.....

<sup>38</sup> Opinion no. 11, to be found at [http://europa.eu.int/comm/european\\_group\\_ethics/docs/avis11\\_en.pdf](http://europa.eu.int/comm/european_group_ethics/docs/avis11_en.pdf)

<sup>39</sup> Strasbourg, 17 october 2002, to be found at [http://www.coe.int/t/e/legal\\_affairs/legal\\_co-operation/bioethics/activities/biomedical\\_research/3intro\\_proposalinstrumentmaterial.asp](http://www.coe.int/t/e/legal_affairs/legal_co-operation/bioethics/activities/biomedical_research/3intro_proposalinstrumentmaterial.asp)



Recital 26 of Directive 98/44/EC on the legal protection of biotechnological inventions  
Mentioned Directive as such is not relevant for the question of consent to 'further use'. The recital, however, states:

Whereas if an intervention is based on biological material of human origin, or if it uses such material, where a patent application is filed, the person from whose body the material was taken must have had an opportunity of expressing free and informed consent thereto, in accordance with national law.

Although a recital as such is not binding, it forms an important interpretative tool for the implementation of a Directive. Therefore it should be discussed here. The background and meaning of recital 26 was clarified by A.G. Jacobs in his opinion in case C-377/98<sup>40</sup> at the points 206-211. What emerges from that discussion is that at least when a patent is envisaged the informed consent must not only relate to the retrieval of the material from the donor but to the possibility of a patent on inventions based upon that material as well.

To complete this overview the coming Directive on 'setting standards of quality and safety for the donation, procurement, testing processing, storage and distribution of human cells and tissues' should be mentioned<sup>41</sup>. It should be stressed that this Directive only bears relation to the standards of the processing of human tissue for therapeutic purposes.

Therefore, in principle this instrument is not relevant to our subject. However, the European Parliament proposed several amendments which are related to research with tissue, even if this research is not aimed at therapeutic use of tissue, which were meant to regulate the ethics of processing tissue of human origin<sup>42</sup>. Most of these proposals have been rejected by the Commission<sup>43</sup>. The Commission argues, on good grounds as it seems to us, that the legal basis of the proposed Directive (art. 152.4 EC Treaty) leaves no room for regulating ethics as such.

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<sup>40</sup> Kingdom of the Netherlands v European Parliament and Council of the European Union. In this case the Netherlands sought – in vain – the annulment of the biotechnological inventions Directive.

<sup>41</sup> COM (2002) 319.

<sup>42</sup> A-5-0103/2003 Final

<sup>43</sup> COM (2002) 340

## 1. Austria

### 1.1 *In general*

Patient rights in general are regulated on several levels. First there is the Law on hospitals and health resorts (KAKuG)<sup>44</sup>. In this law it amongst others stipulated that patients have to be informed in writing about their rights. Second there are the basic requirement for the treatment contract in the Austrian Civil Code. A medical treatment is carried out on the basis of a civil law contract. The obligation that informed consent must be given stems from this 'treatment contract'. Statements of consent do not have to be made in writing, but as a rule operations in hospitals are carried out only after the patient signs a widely used form. This is taken as proof that the patient was informed about and consented to the procedure<sup>45</sup>.

Port mortem organ donation is regulated in the KAKuG. This regulation is based on the opt-out or no –objection system. The 'further use' of left-over tissue is seen as falling under its ambit. Professional secrecy is regulated in the *Ärztengesetz* and sanctioned in the Penal Code as well.

Clinical trials are regulated in two laws, but there is as yet not a general regulation concerning research with human subjects when pharmaceuticals are not involved.

### 1.2 *'Further use' of human tissue*

There is a yet no comprehensive regulation on 'further use'<sup>46</sup>.

Our respondent stated that explicit consent follows from the civil code and the treatment contract. If 'further use' is envisaged it should be discussed with the patient and explicit consent should be obtained. We wonder, however, whether this is the actual practice in Austria at the moment. Our informers did not mention what type of consent would be needed from blanket to for a specific protocol and might not have considered this subject at all.

### 1.3 *Data protection*

#### 1.3.1 In general

The EC Directive has been implemented in *Datenschutzgesetz* 2000. Unlike many other data protection laws this law makes explicit reference to the concept of indirectly identifiable data ('nur indirekt personenbezogen'). These are data where the processor can only

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<sup>44</sup> Bundesgesetz über Krankenanstalten und Kuranstalten.

<sup>45</sup> H.J.J. Leenen, J.K.M. Gevers, G. Pinet, *The rights of patients in Europe: a comparative study*, WHO 1993.

<sup>46</sup> See Decision of the Bioethics Commission of 11-2-2002 concerning the recommendation of Austria's accession to the Biomedicine Convention of the Council of Europe, p. 3..

retrieve the identity of the data subject when using illegal means<sup>47</sup>. We understand that coded data fall under this category.

Section 9 contains the provision for the use of sensitive data<sup>48</sup>. Inter alia use of sensitive data is allowed if and only if this is done with the data subject has unambiguously given his consent (which can be revoked any time) or when this is required for purposes of preventive medicine, medical diagnosis, the provision of health care or treatment or the management of health-care services the use of data by medical personnel or other persons subject to an equivalent duty of secrecy.

### 1.3.2 Data for research

Section 46 of the Datenschutzgesetz 2000 contains the conditions for processing data for scientific research. In general processing data for research is allowed if:

The research is not aimed at arriving conclusions about a particular individual;

Makes uses of either publicly accessible data or data which the processor may use already, or are coded.

In other cases this research should be done:

- pursuant to specific legal provisions, or
- with the consent of the data subject or
- with a permit of the Data Protection Commission.

In the latter case and if sensible data are to be processed, the permit will be granted if:

- the consent of the data subjects is impossible to obtain because they cannot be reached or the effort would otherwise be unreasonable;
- an important public interest is served with the research;
- the data shall be used by persons subject to a statutory duty to confidentiality or whose reliability in this respect is otherwise credible.

The Data Protection Commission may, insofar as necessary, issue its permit subject to terms and conditions.

If the research can be performed with indirectly identifiable data, the data shall be coded without delay. In principle data should be fully anonymised as soon as it is no longer necessary for scientific or statistic work to keep them identifiable.

### 1.3.3 Research with genetic data

This subject is regulated in the separate Act on gentechnology (Gentechnikgesetz). This act regulates the whole range of topics which are related to gentechnology, from genetically modified organisms and the protection of the environment to genetic counselling<sup>49</sup>.

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<sup>47</sup> article 2.1 of the Datenschutzgesetz

<sup>48</sup> which are amongst others data related to the health of the data subject.

<sup>49</sup> And it has even an explicit ban on the use of genetic data by employers or insurers (paragraph 67).

The use of genetic data for research is allowed either with the explicit consent of the source or on anonymised samples. However, samples are considered to be anonymised if they are coded and the researcher does not have access to the name of the source.

Results of the research may only be made public when fully anonymised. (paragraph 66).

## 2. Belgium

### 2.1 *In general*

In September 2002 Belgium adopted a general law on patient rights. This law regulates topics as informed consent, the medical file, representation of incompetent patients, etc. Consent has in principle to be explicit but no written consent is needed except when the patient wishes so. The law does not relate to 'further use' of tissue.

The law on organ donation after death dates from 1986 and is based on an opt-out or no objection system. Donation from living donors (kidney, bone marrow) is regulated as well, but 'further use' of tissue cannot be headed under it. There is a law on the processing of tissue for therapeutic purposes, which again does not relate to 'further use'. No advisory body has issued a statement on 'further use' yet.

According to our source there is no law on research with human subjects. No statement from an advisory body on 'further use' of tissue for research has as yet been given.

### 2.2 *'Further use' of human tissue*

There is no regulation on 'further use'. According to some authors it follows from the treatment contract and its execution 'bona fides' that consent should be given to 'further use'. Others mention that, as data are derived from tissue, data protection legislation should apply. Yet another author has argued in an earlier publication that it is inherent to the visit of a university hospital that left over tissue will be used for teaching or research purposes<sup>50</sup>.

### 2.3 *Data protection*

#### 2.3.1 In general

In 1992 the law on Privacy Protection in relation to the Processing of Personal Data was accepted. This law modified in 1998 following the European Directive. In 2001 secondary legislation in the form of a Royal decree was adopted which especially relates to the use of data for research<sup>51</sup>. The Belgium law considers two types of data: personal data (directly, indirectly and coded data) and anonymous data. This means that coded data remain personal data according to the Belgian law, because the possibility remains to reverse a code, even if not by the processor of the data. The law contains the usual exception to the principle of explicit consent (which even has to be written) to the use of sensitive data when

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<sup>50</sup> For an overview of the discussion see Trouet, o.c. p. 148-152, disagreeing with the last mentioned position.

<sup>51</sup> The law and the decree can be found on <http://www.privacy.fgov.be>. Last checked on July, 28<sup>th</sup> 2003.

this is necessary for – in short - the treatment of the data subject and the processing takes place under the supervision of a health care practitioner.

### 2.3.2 Data for research

Coded data play an important role in the regulation of the processing of data for research. Before they can be transmitted to the researcher these data should in principle be coded. The data subject must be informed about this procedure and can object to it<sup>52</sup>.

The Royal Degree contains an exemption if the data subject cannot be reached or this would be unreasonably difficult. In that case an application to use these data can be made to the Data Protection Commission which can give a permit, if necessary subject to terms and conditions (articles 14-16).

The Royal Degree also contains provisions on the use of non coded data. We will not discuss those as in the ETB project only coded data will be transmitted between the participants.

### 2.3.3 Genetic data

As far as we can see, the Belgian legislation does not contain specific provisions on the use of genetic data for research.

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<sup>52</sup> So, as it seems, even if sensitive data are not involved, this provision is much stricter than follows from Directive 94/46 EC

### 3. England

#### 3.1 *In general*

England<sup>53</sup> is an interesting case as much debate has taken place on 'further use' . The Nuffield Council was probably the first advisory body to issue a report on 'further use' of tissue for research<sup>54</sup>. In a much later stage the debate was heavily influenced by a scandal around the retention of organs and tissue of deceased infants without the consent of the parents. Though this - partially illegal - behaviour did not relate to 'further use' as defined in this report, the following reaction lead to an increased awareness of the public and authorities on the issue of research on left over tissue as well.

As there is much which directly relates to our subject, we will skip regulations like on research on human beings or on organ donation which otherwise might be indirectly relevant. Mention should be made though of the renewed interest in the position of the patient within this system. Several measures were adopted lik: 'Your Guide to the NHS'<sup>55</sup> and the 'Patients' Charter'. The first one has superseded the second one. The NHS has set up the independent Commission for Health Improvement to monitor the quality of care being provided through the NHS. As a result of these measures consent forms for surgical procedures have been introduced in the national health system. It has been suggested that these forms should be used for consent to 'further use' as well. This once again shows the difficulty of 'transplanting' specific solutions of one country to another. In countries were such consent forms are absent, this idea cannot be used.

#### 3.2 *'further use' of tissue for research*

As said an intensive debate has taken place in England concerning 'further use' of tissue for research. The UK Medical Research Council made some sensible recommendations regarding feed back to individual patients as discussed in chapter 2. It proposed a kind of 'layered consent' where a choice is given to the patient for consent to various forms of research.<sup>56</sup> The Department of Health published in April 2003 an interim statement regarding the taking, storage and use of human tissue from the living and the dead pending new legislation.<sup>57</sup>

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<sup>53</sup> We will use the term 'England' here in a somewhat rude way as those known with the local circumstances might prefer to speak of the United Kingdom included or not included Scotland, Wales and Northern Ireland.

<sup>54</sup> Nuffield Council on Bioethics, Human Tissue, ethical and legal issues, London, April 1995.

<sup>55</sup> [http://www.nhs.uk/nhsguide/nhs\\_guide.pdf](http://www.nhs.uk/nhsguide/nhs_guide.pdf). Last checked on August 4<sup>th</sup>, 2003.

<sup>56</sup> [http://www.mrc.ac.uk/pdf-tissue\\_guide\\_fin.pdf](http://www.mrc.ac.uk/pdf-tissue_guide_fin.pdf). Last checked on August 4<sup>th</sup>, 2003.

<sup>57</sup> <http://www.doh.gov.uk/tissue/interimstatement.pdf>. Last checked on August 4<sup>th</sup>, 2003.

The statement proposes written consent for use of left-over tissue for research. It is unclear how specific this consent needs to be probably somewhere between blanket consent and consent specific for one research protocol. About the use of existing stored tissue for clinical research the following was put forward in the interim statement. A decision will need to be taken as to whether consent or further consent need to be sought. Here, three situations can occur:

Valid consent may previously have been given to a particular use or uses, in which case it is usually lawful to use the organs or tissue as already authorised. But consideration is needed whether the form of consent is sufficient on its own to be regarded as valid today.

The donor is identifiable and unambiguous consent has not already been obtained. In that case consent should be sought from the person concerned or if the person is not alive or cannot be traced, from someone close to that person.

The identity of the donor is unknown or the donor cannot be traced. In this case the tissue may in principle be used for research after careful consideration of the possible effects of the research.

The statement admits that the solution for the second group could cause legal and ethical problems. The deceased patient might not have told his/her relatives about his/her decision to donate tissue. The relatives may object to the fact that they have been contacted after losing a loved one many years ago.

The NTRC responded that the interim statement is already less restrictive than earlier proposals. In principle it would be ideal to contact the relatives but this is not realistic in every situation. Ethical review boards have agreed with researchers in some cases that it is not always realistic to receive consent from relatives.

The interim statement also exemplifies problems of comparative legal research and cross boundary medical research. About the first: The interim statement mentions consent for further use forms in addition to the consent for treatment forms. But most countries do not use consent for treatment forms which have to be signed by the patient. About the second: The interim statement argues that tissue which does not comply with the UK rules for consent should not be used in the UK.

Very recently (December 2003) a Bill was proposed to parliament called the Human Tissue Bill encompassing all aspects of the handling of human tissue. With regard to 'further use' of tissue for research and tissue banking the key elements are:

- consent is needed for the use of tissue, whether from living patients or from the deceased, in research. The Bill does not, however, specify what form the consent should take or how and when it should be taken or recorded. As at present, it is envisaged a variety of means by which consent can be given. The new Human Tissue Authority will give guidance on this, taking account of the practical aspects of seeking consent in the course of medical, diagnostic and post mortem procedures;



- The Bill does not specify that consent, when given for research, should be specific to any particular research project. Indeed, it is envisaged that a general consent to research use would be the norm. This would then be subject to the guidance from the HTA and, as at present, to the general standards required by Local Research Ethics Committees in approving research proposals.
- The Bill provides that the use of tissue from living patients for the particular purposes of clinical audit, quality control, 'on the job' education and training, and public health monitoring, will not need consent over and above the consent required for the taking of the tissue from the patient.

To conclude mention should be made of a report on the use of personal genetic information according to which general consent will be sufficient for genetic research, unless the data are directly identifiable<sup>58</sup>. The same approach is taken in the UK Biobank ethics and governance framework<sup>59</sup>.

### 3.3 *data protection*

#### 3.3.1 in general

Data protection is most of all regulated by the Data Protection Act of 1998 (hereinafter the DPA) and following statutory instruments. However the Health and Social Care Act 2001<sup>60</sup> also contains provisions on the processing of medical data and professional secrecy. Data which are coded but are anonymous to the controller are not considered to be personal data in the sense of the DPA (art. 1-1).

#### 3.3.2 Health data for research

The DPA cannot be read without the additional schemes which set out the principles for processing data. Scheme 3 relates to the processing of sensitive data like health data. Processing may take place with the explicit consent of the subject or – as far as relevant in this context – when the processing is necessary for 'medical purposes' and is undertaken by a health professional or a person who owes an equivalent duty of confidentiality. The interesting point is that the term 'medical purposes' includes medical research (art 8 of scheme 3 of the DPA)! No further requirements are necessary.

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<sup>58</sup> K. Liddel, Did the watchdog bark, bite or whimper? *European Journal of Health Law*, 2002, p. 243-256 at 247-248.

<sup>59</sup> September 2003.

<sup>60</sup> <http://www.hmsa.gov.uk/acts/acts2001/20010015.htm>. Last checked on August 4<sup>th</sup>, 2003.

In the statutory instrument of 2000 no. 417 other possibilities are opened for research with sensitive data without the consent of the subject however under the additional conditions (art. 9). The explanatory note refers to archives where sensitive data are held. For health care professionals or persons working in an academic setting with a statutory or contractual duty of confidentiality research with health data will be covered by mentioned art. 8 of scheme 3.

### 3.3.3 Genetic data

There is no provision in the DPA on genetic data.

### 3.3.4 Interim conclusion

The English approach on research with medical data seems very lenient but its importance should not be overestimated in the context of the ETB. If the data are to be derived from tissue, the rules on research with tissue will apply and not those on just research with data. The same holds true if data from tissue are to be enriched with data from other sources. Furthermore recently a code of practice was issued by the Department of Health pertaining to the use of medical data collected in the NHS<sup>61</sup>. We did not have time to study this very recent report.

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<sup>61</sup> November 2003.

## 4. France

### 4.1 *In general*

#### 4.1.1 Preliminary remarks

France proved to be the hardest case to describe in this overview. The first difficulty arises from the fact that the relevant legislation has very recently changed. In 2002 a law was adopted concerning the rights of patients and the quality of the health care system which came into effect on 1-1-2003<sup>62</sup>. This law mainly changes existing regulations, most of all the Public Health Act (hereinafter following the French abbreviation CSP)<sup>63</sup>. A consolidated version of this Act only became available at the end of our survey<sup>64</sup> and some of the necessary by-laws have – as it seems - not been published yet<sup>65</sup>. Other legislation, like the important Law on informatics, records and liberty<sup>66</sup> was recently changed as well. In the second place the French system is rather strictly regulated, to put it mildly<sup>67</sup>. It is hard to ascertain what amidst the hypertrophy of texts – with many cross references - about obligatory notifications, permissions, committees and other official bodies, ordinances etc. really relates to our subject ‘further use’ of tissue, but in the end it seems that most of them do.

#### 4.1.2 Patient rights in general

The right to informed consent was already part of the French law but was more solidly anchored in the legislative texts with mentioned law 2002-303. A brief statement but clear statement about the necessity of informed consent, except in case of emergency, can now be found in article 16.3 of the Civil Code. Articles 1111-2 and 1111-4 of the CSP spell out the necessity of informing the patient in great detail.

Already since 1988 France has explicit regulations on biomedical research on human persons<sup>68</sup>. These regulations are embedded in de CSP as well. They have have been modified since on several occasions lately in the context of the mentioned changes in 2002 and will have to be modified again in the context of the implementation of EC Directive

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<sup>62</sup> Loi no. 2002-303 relative aux droits des maladies et à la qualité du système de santé.

<sup>63</sup> Code Publique de la Santé.

<sup>64</sup> Although most of the French legislation is available on the internet access to the full texts is not possible in the case of the ‘grands codes’. The revised version of the Dalloz Edition of the Code de la Santé Publique with the major 2002 changes incorporated became available at the end of march 2003.

<sup>65</sup> See section .....

<sup>66</sup> Loi no 78-17 relative à l’informatique, aux fichiers et aux libertés

<sup>67</sup> to put is less mildly, it seems to be the bureaucrat’s paradise

<sup>68</sup> Law 88-1188 of 20-12-1998 (Loi Huriet-Séclat).

2001/20<sup>69</sup>. Research with left over tissue cannot be seen as falling under the ambit of these regulations as they deal with research 'on' (in French "sur") human beings. The regulations contain, amongst others, the instalment of several 'ethical review boards'<sup>70</sup>. These operate on the regional or municipal level according to the size of the population. The members are appointed by a state's representative for the region for which the committee is authorized<sup>71</sup>. At the beginning of 2001 there were 48 of these committees<sup>72</sup>. A report of the French senate (note 73 ) shows that in many cases they are asked to give an advisory opinion on a draft protocol before it officially submitted to them. It would be interesting to know whether these committees also fulfil a role for the review of research which does not fall under the type of biomedical research for which they are appointed.

French has a detailed provisions concerning organ donation. Organ donation after death is based on the opt-out or no objection system (L 1232-1 of the CSP). .

## 4.2 *'Further use' of human tissue*

### 4.2.1 In general: the storage of human tissue for research

There is a specific chapter in the CSP about the 'harvesting' of tissue for therapeutic use<sup>73</sup> or research. Most of provisions in this chapter relate to an envisaged therapeutic use. When they relate to scientific use they are caught in such general terms that they seem to be applicable to 'further use' as well, even though the chapter as such is devoted to tissue which is specifically taken out for either therapeutic or scientific use.

This is the case in art. 1243-2. A public or private entity may conserve and process tissue for research which follows from its research program but should notify the Minister for Research first. The Minister may refuse this handling of tissue if there are insufficient safeguards concerning the protection of employees, the environment or the fundamental values described in the first chapter of the CSP. We will come back to this latter aspect in the next section.

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<sup>69</sup> See P. Jaillot, J-P Demarez, Editorial in La Lettre du Pharmacologue may-june, 2003.

<sup>70</sup> Comités consultatives de protections des personnes dans la recherche biomédicale.

<sup>71</sup> The candidature of the members has to be put forward by specified bodies according to the discipline of the member. For the lawyer in the committee these should be amongst others the President of the Court of Appeal or the presidents of the universities in the regions.

<sup>72</sup> Senat, 2000-2001, no. 267, Rapport d'Information au nom de la commission des affaires sociales sur le fonctionnement des comités consultatifs de protections des personnes dans la recherche biomédicale.

<sup>73</sup> Meaning that the tissue whether or not in a processed form will be used again on human like bone grafts.

If the research is performed on the same site where tissue is handled for therapeutic use the French health Products Safety Agency<sup>74</sup> should be informed as well which may uphold or interdict the research.

In another chapter of the CSP there is a separate clause on tissue banks (L 1131-4). It says that if tissue is taken out from a specific group with the aim of doing genetic research on the thus assembled tissue the research project should be declared to the competent administrative authority first. Existing collections should be notified to this authority within a delay of six months. However, as it seems, this authority does not seem to exist yet<sup>75</sup>.

To conclude brief mention should be made of a recent report of the French National Consultative Bioethics Committee for Health and Life Sciences<sup>76</sup> on 'biobanks'. It stresses the need for 'free and informed consent' at the same recognising the complexities of such a position as not all research can be spelled out in advance. It also mentions 'solidarity' and 'altruism' as values which should be taken into account, which is rarely seen in other reports on the issue. Though the report makes some firm statements, it is exploratory as well and points at the necessity of further discussion and research on the topics addressed in it.

#### 4.2.2 Consent for 'further use' ?

We did not find any provisions which are directly related to 'further use', apart from L 1245-2 of the CSP. This article states that basic rules about the non commerciality of donating tissue and the anonymity of the donor apply to 'further use' of tissue as well.

The interesting point is whether the newly incorporated clauses on the rights of patients, with amongst others, the elaboration of the informed consent principle, apply to 'further use' of tissue as well.

As seen, art. L 1243-2 refers to this part of the CSP. However, this might also be seen as referring to the taking out of the tissue with a research goal which is the intended scope of this article. Trouet<sup>77</sup> admits that in the original (before the 2002 changes) system no consent was needed for 'further use', but states that the new emphasis on patient rights leading to the Act on this subject (see section 12.1) has changed this.

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<sup>74</sup> Agence française de sécurité sanitaire des produits de santé. This agency plays an important role in the provisions relating to therapeutic use of tissue.

<sup>75</sup> J.P. Demarez, internet publication found on :

<http://chusa.b3e.jussieu.fr/urcest/EC/legislation/fajjpd.htm> (last visited on 18 October 2003).

<sup>76</sup> Comité consultatif national d'éthique pour les sciences de la vie et de la santé, Avis no. 77, Febraury 2003.

<sup>77</sup> Oc. p. 217-219.

This contention does not follow from the text of the CSP. The most logical translation, from a systematic legislative point of view, would have been to extend the referrals in art. L 1245-2, which is far as we can see the only article which relates to 'further use', to the first Title of the CSP as well. In this first Title the basic rights of the patient, like that on informed consent, are laid down. This has not happened. From our position we cannot see whether this was an incidental omission or was done on purpose. Considering the thoroughness of the legislative change the first position seems more plausible. From that it would follow that no explicit consent for 'further use' is necessary. It should be stressed, however, that the literature, quoted by Trouet, has a different opinion. This literature dates from before the 2002 legislative changes.

At the same time it should be clear that the provisions on the information which should be given to the patient when entering a health facility or in the course of his/her treatment are quite extensive and go beyond the mere informed consent for a decision whether or not to undergo a medical procedure. It therefore seems to follow that if the facility knows that tissue may be used for 'further use', it should notify the patient in the general information. As such a notification is rather senseless when the patient cannot react to it, at least an opt out system seems to be (least) option for 'further use' according to French law.

#### 4.2.3 Speciality: the necessity of a permit ('authorisation') to import or export tissue

Contrary to all other countries in this survey, French scientist need a permit to import or export tissue for research. This is laid down in art. L.1254-4 of the CSP and further elaborated in By-law<sup>78</sup> no. 2000-156. The dossier which has to be transmitted to the Minister of research in order to get the permission seems to be quite elaborate.

We will come back to this topic in the last chapter.

### 4.3 *Data protection*

#### 4.3.1 In general

The French data protection law dates from already 1978<sup>79</sup> but has of course since then been changed on several occasions.

Data which are coded but anonymous to the controller are considered personal data<sup>80</sup>.

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<sup>78</sup> Décret en Conseil d'Etat.

<sup>79</sup> Loi no. 78-17 relative à l'informatique, aux fichiers et aux libertés.

<sup>80</sup> Explanation to art. 4 : Est donnée nominative toute donnée permettant directement ou non d'identifier une personne : noms, listes comportant un moyen d'identification (numéro de code, initiales, prélèvement biologique identifiant), renvoyant à une grille de référence, recoupement

#### 4.3.2 health data for research

There is a separate chapter on this subject (V bis). Summarising the system is as follows:

- studies based on data collection of the individual follow-up of patients are not considered to be research in the sense of this chapter;
- the proposed research has first to get an advice from a committee established at the Ministry of Research;
- then it has to get the approval of the French data protection authority which may take 6 months for its decision (can be prolonged with another six months);
- In principle directly identifiable data should be coded before they can be transmitted for research. This obligation can be waived for certain studies, like pharmacovigilance, or if the methodology of the study would make this necessary;
- Everyone has the right to oppose to the use of his or her data in research;
- Subjects should give specific consent to the study if the data are collected directly from them or from their medical dossier. The only exception to latter rule seems to be if the therapeutic exception has been applied by the treating doctor;
- If the data were originally gathered for another goal than treatment the obligation to ask consent may be waived if it would be nearly impossible to retrieve the data subjects. The data protection authority has to approve this on the basis of the arguments given in the dossier;
- Information about the possible use of data for research should be available in every health care facility;
- The use of non coded data for research outside France will be refused if the other country does not offer the same protection.

The system seems strict. We were unable to find the Bylaw (Décret en Conseil d'Etat) which further regulates the modalities of the system.

#### 4.3.3 Genetic data

Genetic data are not treated differently in mentioned chapter which is logical as it seems hard to imagine how they could be treated stricter than the already very strict provisions for medical data in general.

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d'informations si la population concernée est d'effectif restreint (date et lieu de naissance, résidence, pathologie).

## 5. Italy

### 5.1 *In general*

The situation in Italy seems fairly easy to describe as there little specific legislation on the subject. At the same time this complicates the description as the rights of the patients are recognised in other kinds of documents like the elaborate deontological Code of the medical profession<sup>81</sup>. The right to informed consent of the patient can be found in this document (articles 30-32).

Until recently there was no legislation on medical research on human beings. Mentioned deontological code has provisions on this subject as well. Following Directive EC 2001/20 the Italian Council of Ministers adopted a Legislative Decree in June 2003 to implement the Directive.

There is a law on organ donation<sup>82</sup> which has a kind of reversed opt out system. Persons are requested to express their willingness to donate after death in a national registry or in the personal medical record. Of those who have expressed their willingness organs may be used for donation (therapeutic use) after death. This may also be the case if after the request one hasn't declared anything in the national registry and does not carry a signed document that one refuses organ donation (articles 4.4 and 4.5). If no request has been made to someone be considered as a donor (art. 4.2).

### 5.2 *'Further use' for research*

There is no regulation on the subject. It is not addressed in the deontological Code either. As far we can see no discussion has taken place in the literature.

### 5.3 *Dataprotection*

#### 5.3.1 In general

The Italian law on data protection dates from 1996<sup>83</sup>. Data which are anonymous to the controller but which are coded are considered personal data in the sense of this Act (art. 1.2 under c).

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<sup>81</sup> The newest version was approved in 1999. It was handed over to us and we cannot give a proper reference with regard to the editor.

<sup>82</sup> Law of april 1999, no. 91.

<sup>83</sup> Law of 12 december 1996, no. 675.



### 5.3.2 Health data for research

The Act has been elaborated in several Ministerial Degrees. For our purpose most of all important is Decree nr. 281 of July 28<sup>1</sup> pertaining to the processing of personal data for historical, statistical and research purposes.

The general system for using personal health data for research seems<sup>84</sup> to be as follows. Research on health data is possible with explicit consent of the subject and a permission of the Italian data protection authority called the 'Garante'. Use of these data without consent is only possible if the subject cannot be found and there is a pressing public interest involved in the research.

### 5.3.3 Genetic data

For the use of genetic data even stricter provisions apply. The permission will only be granted after an opinion of the Minister for health who must hear the High Health Council first.

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<sup>84</sup> This section is largely based on an article in the European Journal of Health Law, A. Bompiani, Genetic data and regulations of personal data in Italy, 2001, p. 41-50. We have found some of the degrees mentioned in this article but we were unable to retrieve all. A request for the original text at the 'Garante' remained unanswered.

## 6. The Netherlands

### 6.1 *In general*

In the second half of the 1990'ties several Acts on patient rights came into force. The main Act is the Act on the treatment contract (hereinafter following the Dutch abbreviation the WGBO) which became part of the Dutch Civil Code in April 1994. Amongst others the WGBO has explicit provisions on information and consent.

The act on research involving human subjects came into force a few years later (hereinafter following the Dutch abbreviation: WMO). This Act covers all interventions on or requesting specific actions of human beings with the aim of performing medical scientific research. From this definition it follows that 'further use' of tissue is not covered by it. The WMO has been inspired by the French Act on research with human beings. It uses a decentralised system of ethical review boards which must approve a protocol before it may start. In many cases these IRB's are requested to give an opinion or advice on research which does not fall under the ambit of the WMO, like research on already existing tissue ('further use'). The WMO will be amended following Directive EC 2001/20. An amending Act has already been approved by the second chamber of the Dutch parliament.

The Dutch law on organ donation came into force about the same time as the WMO. For donation after death it is based on the so called 'full decision system'. This means that everyone is requested to submit to the national registry the decision whether he/she wants to donate organs, in which case specific organs may be named, or refuses. If no decision has been made by the deceased the next to kin may decide. As most persons did not register anything and relatives tend to refuse organ donation in these cases, the new Act lead to a decrease in the availability of organ donation after death. Other factors have influenced this decrease as well, like better road safety, but nevertheless the debate has started again whether 'the full decision system' shouldn't be replaced by the opt out or no objection system of countries like Belgium, Austria and France.

### 6.2 *'Further use' of tissue for research*

After a heated debate about anonymous HIV prevalence screening a clause was inserted in the then draft WGBO stating that 'further use' of anonymous tissue for scientific or statistical purposes may only take place if the source has not objected to such use.

No explicit provisions exist concerning research with anonymous but coded tissue and directly identifiable tissue. There is consensus amongst health lawyers and researchers that for the latter category explicit consent is needed<sup>85</sup>.

The debate at the moment is about the in between category of anonymous but coded tissue. Many health lawyers follow the Advice of the Dutch Health Council, issued in 1994<sup>86</sup>, that consent is needed for this kind of 'further use', though this may be a kind of blanket consent. The Code of Conduct of the Dutch Federation of Medical Scientific Organisations uses the no objection system. Connected with this system is an opt in possibility for patients who want individual feed back of results of the research which might be of direct relevance to them or their relatives.

A legislative proposal on the subject has been announced by various governments on many occasions but has never appeared yet. It has once again been announced for the beginning of 2004.

### 6.3 *Data protection*

#### 6.3.1 In general

The Dutch regulations concerning the of medical data in research are both complex and fairly simple. They are complex as the provisions of the WGBO and the Dutch Act on the protection of personal data (hereinafter after the Dutch abbreviation: the WBP) have to be read together. They are fairly simple as they do not involve special procedures or permits to work with certain data as can be seen in some other countries.

First of all it should be noted that in the Dutch situation the concept of personal data does not mean data which are anonymous to the controller but may be linked to the identity of the source by third party via a code which is added to these data. This standpoint has been contested by some health lawyers but is still the official point of view, also from the Dutch Data Protection Authority<sup>87</sup>.

So personal data have to be directly or indirectly identifiable by the controller. If they are only indirectly identifiable by someone else, they are anonymous data to the controller. At the same time the Dutch interpretation of indirectly identifiable is rather strict. If there is a remote change that the controller can link some of the data to the identity of the subject, the data will be considered indirectly identifiable and hence personal data even if the

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<sup>85</sup> See the Code on Proper Use of Tissue of the Dutch Federation of Medical Scientific Organisations (available at [www.fwmv.nl](http://www.fwmv.nl)) and the comment of E. Olsthoorn in TvGR 2003, p. 306-313.

<sup>86</sup> The Hague, 1994.

<sup>87</sup> for an overview of the discussion and the various concepts of anonymous, coded, indirectly identifiable data see E-B van Veen, Gecodeerde gegevens en wetenschappelijk onderzoek, Privacy & Informatie, December 2003 (in print).

controller or those working under his supervision would have to use extralegal means for this linking.

### 6.3.2 Health data for research

The basic rule for using personal health data in research is that the data subject must have given consent. There are two exceptions to this rule:

- Directly identifiable data may be used without consent if it proves impossible to ask consent from the patient;
- Indirectly identifiable data may be used if it can be shown that it is infeasible to ask consent from the patients.

Both situations have been elaborated in a Code of Practice for researchers working with medical data which was approved by the Dutch Data Protection Authority<sup>88</sup>.

Situation 1 arises when the patient has died, cannot be retrieved after seriously trying to do so or does not respond to repeated requests for permission. It also encompasses situations where because of the long interval between the research and the disease and the seriousness of the previous disease re-contacting the patient might create serious psychological problems for the patient or their relatives<sup>89</sup>.

Situation 2 arises when such large samples of the population are used that the project would become impossible if consent should be sought, either because of the costs or because one would arrive in situation 1 for many of the subjects anyhow. The code of practice uses for this situation the concept of coded indirectly identifiable data. This system makes it possible to reconcile mentioned strict (or broad, depending on how you look at it) interpretation of indirectly identifiable with the necessity of linking data from various sources or subsequent data from one source to a single data subject.

Additional requirements apply to make use of the exceptions. These are translated in mentioned Code of Practice. One of them is that an ethical review board must have approved the research project. No permit from the Data protection authority is required. With the workload of the official WMO ethical review boards for the approval of WMO trials, researchers encounter increasing difficulties to find such boards prepared to consider their protocols which just make use of existing data.

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<sup>88</sup> The first Code already in 1995 under the forerunner of the present data protection Act and Authority. The new version will be approved at the end of 2003.

<sup>89</sup> This exception has been inserted in the Code of Practice after an research project where researchers re-contacted former cancer patients to ask permission to use additional data and many of these patients, if still alive, reacted with utmost concern thinking that the disease might come back, although the letter carefully avoided that suggestion.

### 6.3.3 Genetic data

There is no specific provision for genetic data in the Code of Conduct as the WBP does not require this. The WBP has a provision on the use of genetic data (art. 21.4) which states that genetic data may only be used with regard to the person from which they are derived, except in the case of genetic counselling. This clause is directed against insurers and the like and does not relate to research with such data.

## 7. Spain

### 7.1 *In general*

Recently (May 2003) the law on patient rights came into force<sup>90</sup>. This law underscores the principle of informed consent, regulates, like in other countries, substitute decision making for those who cannot consent and such subjects. It does not bear directly to 'further use'. There are laws on medical research involving human subjects (dating already from 1993) and on organ donation which is based on the opt out system. Neither of them is relevant for our subject. However, it seems that as in some other countries the ethical review boards organised for the approval of trials also consider 'further use' of tissue. Our correspondent mentioned that the terms of reference in such cases is the regulation of clinical trials which is not always adequate to give an opinion on a protocol with just 'further use' of tissue.

### 7.2 *'further use' of tissue for research*

There is no regulation on this subject and neither have there been promulgated statements from authoritative bodies.

### 7.3 *Data protection*

#### 7.3.1 In general

The Data protection law, implementing EC Directive 96/46 came into force 1999<sup>91</sup>. The definition of personal data repeats the definition of the Directive. We have not been able to find out whether coded data which are anonymous to the controller are considered personal data or not under the act.

#### 7.3.2 Health data for research

Health data may be processed in the health care system for the diagnosis or treatment of the patient subject to the national and regional legislation on health care (art. 8). We did not investigate that legislation. There general rule for processing health data outside that health care is consent of the subject concerned (art. 11.1). There is an exemption for conducting epidemiological studies within the meaning of the central or regional government health care legislation (art. 11.2 under f). Again we did not investigate that legislation.

#### 7.3.3 Genetic data

We did not find any provision on genetic data and its existence was not reported to us either.

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<sup>90</sup> Law 41/2002.

<sup>91</sup> Law 15/1999

