

## **COMMENTS on the draft CIOMS International Guidelines for Ethical Review of Epidemiological studies**

Drafted on behalf of the Dutch Epidemiological Society and the Federation of Dutch Biomedical Societies

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These comments may be used for its intended purposes by epidemiological organisations. When used by others or for other purposes they should be cited as: E.B. van Veen, Comments on the draft CIOMS Guidelines for Ethical Review of Epidemiological Studies, Medlawconsult, The Hague, 2005 [www.medlaw.nl/documenten/comments.pdf](http://www.medlaw.nl/documenten/comments.pdf) (available as from November 1 2005)

## 1. Introduction

### 1.1 *About the Dutch Epidemiological Society and the Federation of Dutch Biomedical Societies*

The Dutch Epidemiological Society (VvE) is the professional society for Dutch epidemiologists. It has about 1200 members. The Federation of Dutch Biomedical Societies (FMWV) is the umbrella organisation for societies like the VvE. Via their respective professional societies about 12000 researchers and professionals in health care are represented by the FMWV. The mission of the FMWV is to further the interests in biomedical and health research in a balanced way. To safeguard its independence it does not receive government funding. Funding from industry is only admitted for specific, temporary projects and then of course in a transparent way and in accordance with the regulations on advertising by pharmaceutical industry.

'Self regulation' by way of Codes of Conduct is one of the activities of the FWMV. Such Codes of Conduct are always drafted together with other stakeholders, like patient organisations and the Royal Dutch Medical Association.

In 2002 the FWMV is issued a Code of Conduct on 'further use' of human tissue for research. In 2004 it issued a Code of Conduct for research with medical data. The Dutch Data Protection Authority declared this Code of Conduct to be in conformity with the Dutch Data Protection Act and the Act on the medical treatment contract. Both Codes of Conduct can be found on the site of the FMWV under Codes of Conduct.<sup>1</sup>

### 1.2 *About the author*

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### 1.3 *About these comments: purpose and limits*

Hereinafter I will refer to the draft Guidelines simply as Guidelines.

The purpose of these comments is to provide concise background information for a possible policy statement of the Dutch Epidemiological Society or the IEA/EF on the Guidelines. These comments do not claim to be a full review of the Guidelines and have been written under budgetary and time constraints. As the Guidelines touch upon many delicate subjects, it could not be avoided that these comments cover several pages. The Guidelines seem to be unaware of many aspects of the present and to my view balanced regulatory regimes on epidemiological research, and therefore I had to explain these in some detail. Otherwise the comments would probably not succeed in counter balancing the views expressed in the Guidelines. Yet, I have tried to be as brief as possible. References to literature have only been added when strictly necessary. In order not to interrupt the main text extra explanation is given in some of the footnotes.

Background information could be provided from many angles. I choose to explain the possible consequences of the Guidelines for European epidemiological research. The Guidelines contain many remarks on global equity in the burdens and benefits of research. These are not discussed.

<sup>1</sup> [www.fmwv.nl](http://www.fmwv.nl) (the site does not show the links to specific pages).

<sup>2</sup> [www.tubafrost.org](http://www.tubafrost.org) (the site is at this moment largely under construction)

<sup>3</sup> <http://www.virgil-net.org>

<sup>4</sup> <http://www.medlaw.nl/en/english.html>

To be as brief as possible, I did not discuss the Guidelines line by line, but took the main themes and some striking differences with present regulatory approaches in Europe and to a lesser extent in the US.

Two of these themes have been explained at length in the paragraphs 4 and 5. Conclusions have been added there. As the other paragraphs were much shorter, no conclusions were formulated at the end of these paragraphs.

Unless stated otherwise all cited websites have last been visited between 20-25 October 2005.

## 2. Some background information on the Guidelines

### 2.1 About CIOMS

CIOMS stand for Council of International Organisations of Medical Sciences. It is a non-governmental organisation established by the WHO and Unesco in 1949.

According to its website ([www.cioms.ch](http://www.cioms.ch)) the main objectives of CIOMS are:

- “To facilitate and promote international activities in the field of biomedical sciences, especially when the participation of several international associations and national institutions is deemed necessary;
- To maintain collaborative relations with the United Nations and its specialized agencies, in particular with WHO and UNESCO;
- To serve the scientific interests of the international biomedical community in general.

To achieve its objectives, CIOMS has initiated and coordinates the following main long-term programmes:

- Bioethics
- Health Policy, Ethics and Human Values - An International Dialogue
- Drug Development and Use
- International Nomenclature of Diseases “

The latter program seems to be ended. Certain international organisations can become member of CIOMS. The IEA is not a member. The Statutes of CIOMS which explain which organisations are eligible for membership can not be found on the website.

### 2.2 The ‘Core Group’

The present draft Guidelines have been drafted by a ‘Core Group’ composed as follows: M. Valotton (Swiss Academy of Medical Sciences, President CIOMS), A. Capron (WHO), R. Saracci (IARC/WHO), H. Peterson (WHO), E. Vayena (WHO), S. Niu (ILO), I. Matsedu (Science Council of Japan), J. van Delden (KNAW, Netherlands), J. Rantanen (Institute of Occupational Health Finland, Int. Commission on Occupational Health), J.E. Idänpään-Hekkila (CIOMS), S.S. Fluss (CIOMS).

In the introduction this group is described as a “group of experts” but it appears to be mainly composed of civil servants from international organisations.

### 2.3 About the status of CIOMS guidelines

Such guidelines are not binding law. They form part of the rapidly growing body of international pseudo-law on biomedical issues. From the perspective of democratic theory questions can be asked about this proliferation of international pseudo-law.<sup>5</sup>

Between these international guidelines, recommendations, etc. a certain ranking seems to exist. That ranking is not based on any official legal hierarchy but more on the status of the organisation who issued the guidelines or whatever they are called. CIOMS issued new guidelines on Biomedical research in 2002 (hereinafter referred to as the general Guidelines). They are hardly ever cited.

The present 1991 guidelines on epidemiological research are cited even less. I wonder whether epidemiologists are even aware of them. However, this might change under the

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<sup>5</sup>E.B. Van Veen, Regulatory issues of exchanging tissue for research: largely a non-issue? EJC submitted for publication.

new Guidelines. The general Guidelines have to 'compete' with many other international instruments on interventional biomedical research. As far as I know, there are no international instruments on epidemiological research as such.

#### 2.4 *A few critical remarks about the drafting process*

International instruments like these cannot be drafted in conformity with the democratic process as we know it at the national legislative level. Lacking that, the process should comply with which is commonly accepted as the next best solution: transparency about the process. Such transparency means that drafts are announced and can be found on the website, that relevant stakeholders are invited to comment and that clear and objective procedures exist how these comments shall be weighed and who will finally approve of the guidelines.

Only very recently, about two-three weeks before the official closing time for comments, the draft of the Guidelines could be found on the CIOMS website.<sup>6</sup> It does not state how comments will be weighed, what the next steps will be, how the core group of 'experts' has been selected, etc.

One can only wonder why the 'transparency principle' is only partially adhered to and the IEA or IEA/EF as the main stakeholder has not been asked to comment on a draft in a much earlier stage.

### 3. The definition of epidemiological research

#### 3.1 *In general*

A definition of epidemiological research is lacking. The guidelines cover a whole range of subjects, 'epidemiological' research with drugs, with data, with tissue samples, 'interventional epidemiological studies', and observational research. Reading the Guidelines one wonders what is not epidemiological research. It sometimes seems as if texts from the general Guidelines have been 'copy-pasted' indiscriminately into the epidemiological Guidelines.

#### 3.2 *Epidemiological research 'involving human subjects'*

Apart from the problem of the definition of 'epidemiological', the Guidelines are limited to such research involving human subjects. It mentions that research involving human subjects includes research with identifiable human tissue and data. Without referring to it, this tenet is derived from the WMA 'Helsinki Declaration' as amended in 2000 (Edinburgh revision).

Of course, this raises the questions when data are identifiable. The Guidelines do not give a definition of this either. I will discuss that complicated issue (better, it has been made complicated) in the next paragraph. Much depends on that definition. But even if the data are by all standards 'identifiable', the idea that people who participate in an epidemiological study always should be considered 'human research subjects' seems contrary to accepted European standards. As the Guidelines are based on this idea and this idea defines the scope of application of the Guidelines, I will discuss that issue here.

#### 3.3 *'Human research subjects' in epidemiological research*

All European data protection and – if there is such legislation – patient rights legislation leave room for research with patient data, though under various conditions. Nowhere in such regulations or in the statements of the supervisory bodies the patient becomes a 'research subject' when his data are used in research.

In (epidemiological) panel studies the participants are considered to be, like I said, participants. Not research subjects. In Europe the term research subject is, is usually restricted to interventional research or observational research where the participant is subjected to such a regime that it amounts to an intervention. A simple questionnaire or

<sup>6</sup> <http://www.cioms.ch/epiwebdoc.pdf>

even membership of a panel is not considered to be 'an intervention'. Extracting data from patient records is not considered an intervention either.

The phrase 'human research subject' for all those uses is US parlance. It stems from the Code of Federal Regulations (CFR) which in short considers all research 'human subject research' when the researcher obtains data from an intervention or interaction with the individual or obtains identifiable private information. (I will discuss the interpretation of 'identifiable private information' in the next paragraph).

To me there seems a danger in accepting the US parlance in the European situation, even though, as we shall see in the next paragraph, in the US situation 'identifiable' can be described quite narrowly.

The danger is most of all that two distinct categories of research are confounded which hitherto have been clearly distinguished on the European level, namely research which involves an intervention in the broadest sense and research which does not do so. The first type of research is described as human subjects research and always requires a positive 'risk- benefit' (or, according to the CIOMS guidelines '(potential) harm-benefit' ratio) together with a.o. a complicated informed consent procedure. The latter type of research is not considered human subject research and less strict tests for performing the research are acceptable.

It should be mentioned that in the US situation more or less the same result is reached via another route, namely by applying 'the minimal risk, minimal burden test' on all human subject research. If the research meets mentioned criterion, the prerequisites for doing that research are also be much less rigorous.

So in Europe the definition of the type of research determines the conditions under which it can be performed. Non interventional research is considered minimal risk and minimal harm research by definition and another regulatory regime applies. The possible risks are considered under the aegis of data protection legislation. In some countries specific legislation of the use of human tissue samples has been enacted (see paragraph 7 hereinafter).

In the US everything is human subject research but after applying mentioned criterion the prerequisites are to a certain extent comparable.<sup>7</sup>

If these distinctions are ignored, one gets a confused situation and even more so if the US restricted interpretation of 'identifiable' is not applied (see the next paragraph). The CIOMS guidelines, in the wake of the WMA declaration, ignore these distinctions. This leads to a rhetoric of 'human subject protection' and protection schemes are piled upon each other. I will give some examples in paragraphs 5 - 8.

### 3.4 Conclusions

- The Guidelines do not define epidemiological research.
- Neither do they define 'identifiable data and human tissue samples'.
- The scope of application of the Guidelines is therefore unclear to say the least.
- Use of 'identifiable data and tissue' would according to the Guidelines be 'human subjects research'. This is in line with the US definition and the WMA Helsinki Declaration after the 2000 (Edinburgh) revision but not with the European interpretation of human subjects research.
- It is dangerous to adopt this US parlance on the European situation as the regulatory regime in Europe is very different. Observational research in Europe is most of all covered by data protection legislation.
- When the US parlance would be used, then one should also use the differentiations made in the US between types of "human subject research" and the relaxation of certain requirements for 'minimal risk, minimal burden research' together with the

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<sup>7</sup> The US Health Information Portability and Accountability Act has complicated this scheme in a practical sense but mentioned basic distinctions are not altered by it. HIPAA will remain out of the scope of this report.

narrow definition of identifiable data (and human tissue samples). However, nothing of that kind is done in the Guidelines.

#### 4. Identifiable data (and human tissue samples)

##### 4.1 *In general*

There is considerable confusion on this subject, both about definitions (see the next section) but also on the approach followed. This approach can be legal or theoretical. With legal I refer to an approach which investigates how data are considered or can be used for research in a certain legal system under certain conditions. With theoretical I refer to an approach which starts from one's own ideas about types of data and how they should or should not be used in research.

I will use the legal approach, as theoretical approaches can provide an interesting frame of reference, also for discussing national law, but cannot override it. And neither can theoretical distinctions made in international non-binding Guidelines.

What is said here about data applies to human tissue as well. Human tissue is "data plus". Data always accompany the tissue. The 'plus' is a certain extra sensibility attached to tissue, the fact that new data can be derived from tissue and that research on tissue can lead to patents. Only the middle point needs to interest us here. Tissue is from that point of view an extra set of data. However, it does not change its status according to the definition given to the attached data. If the data attached to the tissue are fully anonymous (implying that nobody can reasonably retrieve the identity of the patient from these data) data derived from the tissue are anonymous as well.<sup>8</sup>

##### 4.2 *Definitions*

Knoppers and Saginur have quite rightfully argued that a Babylonian confusion exists around the terminology for genetic data.<sup>9</sup> This applies to non genetic data as well. However, whatever the differences, they are variations on the theme and use more or less the same phrases. The Guidelines give definitions as well (under guideline 18). Completely different phrases are used there which seem to stem from another planet. I will discard them in what follows.

Hereunder I will make the more usual distinctions. I will give each category a name (and a number) but others sometimes use different names. This is slightly confusing but not a major problem if a description is given what type of data one is referring to. What should interest us most of all what regulatory regime applies to each distinct category, insofar as relevant for appreciation of the Guidelines (as a lot more could be said about this subject). The legal consequences will be discussed in the next section.

1. Directly identifiable data: the researcher has the name, address etc. of the subject or has access to these data;
2. The researcher has no directly identifiable data but the data are on such an aggregation level that he could retrieve the identity of the data subject without using

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<sup>8</sup> Of course, it has been argued that the genetic profile derived from the tissue can be matched with other profiles with identifiable data and so tissue is always identifiable. I will discard this scenario which is simple impossible in the context of research in states where the rule of law reigns. And if in exceptional circumstances authorities want to lay their hand on certain tissue for forensic purposes, that tissue will be much more readily available with probably much more identifiable data attached to it outside the research laboratories. It is another issue that linking large databases encompassing large parts of the population with type 3 or 4 (see the next section) data could result in type 2 or even type 1 data. If these databases contain genetic information then genetic information will become available as well. This is an important issue which, however, is related to the protection of these databases, not to some 'inherent identifiability' of human tissue as such.

<sup>9</sup> B.M. Knoppers, M. Saginur, The Babel of genetic data terminology, 8, Nature Biotechnology, 2005, 925-927.

'unreasonable' means. In many European jurisdictions full zip code, birth date and gender are considered type 2 data. They are usually referred to as indirectly identifiable data;

3. Anonymous data: the researcher can not, without using unreasonable means, retrieve the identity of the data subject.

The dividing line between 2 and 3 is not sharp. It can be a matter of appreciation whether certain data should be classified under 2 or 3.

Next there is another category, namely:

4. Type 3 data which have a codenumber attached to them. The researcher does not hold the key to the code. The codenumber is attached by the provider of the data through – usually – some algorithm program which transcribes the direct identifiers into this number. I will refer to them as anonymous but coded data.<sup>10</sup>

Two types of coding exist, namely 'one way coding' and 'two way coding'. With one way coding it is only possible to transcribe the identifiers into the codenumber. With two way coding the reverse is possible as well. It should be underscored that this can only be done by the key-holder, who is, by definition for this type of data, not the researcher. Hereinafter when I refer to type 4 data, I refer to two way coded type 3 data.<sup>11</sup>

One way coding does not change the status of type 3 data. There is considerable discussion whether two way coding does. Different jurisdictions give different answers to this question.

#### 4.3 *How are these distinctions used to decide whether data are identifiable or for determining the applicable regulatory regime for that kind of research?*

##### In the US

As seen in the previous paragraph the two questions of this section coincide there (leaving aside, as I will do, HIPAA). The question whether data are identifiable determines whether the regime of human subject research is applicable.

In a 'Guidance on Research Involving Coded Private Information and Biological Samples' of August 2004 the US departmental Office for Human Research Protection stated, in short that type 4 data (and tissue samples) are not considered identifiable in the sense of the mentioned section of the CFR. therefore the use of type 4 data does not constitute 'human subject research'.

This is very important conclusion for the use of US parlance about 'human subject research'. The practical implications of this parlance are limited to research with type 1 and 2 data. Type 4 data (and tissue, which is the majority) is not covered by it. And type 2 data will usually be covered by the 'minimal harm, minimal burden test'.

However, the Guidelines do not seem to recognise this. Though a definition of 'identifiable' is not given, they seems to encompass type 4 data and tissue.

##### Europe

In Europe the answer to the first question of this section is quite complicated.<sup>5</sup> I have added in an appendix an excerpt of a publication I am working on regarding this subject.

It comes down to the fact that some countries regard type 4 data as 'personal data' and other don't.

<sup>10</sup> By some they are also called indirectly identifiable or coded linked. Indirectly identifiable is confusing as it can refer to type 2 data as well. Linked is confusing as it is not neutral. It suggests that the results of the research can be linked to the individual but this will depend on the conditions under which the data were transferred and the research is performed.

<sup>11</sup> In the biomedical ethics literature one sometimes sees mentioned 'single' and 'double coding'. These are not the terms which the ICT literature uses for the procedures mentioned in the text.

However, this is of less importance in Europe as the two questions do not coincide. There are traditionally different regulatory regimes for the use of data for research, the use of tissue for research and human subject research as understood in the European context, being interventional research.

And with regard to data, in most systems patient data which are considered personal data in the sense of the Directive, can be used for epidemiological research without the consent of the patient. This even applies, under certain circumstances, to type 1 data. The European Data protection Directive (95/46 EC) left room for exceptions on the consent principle for the use of data for research. In all member states this possibility has to varying extent been used in their national data (and patient rights) legislation.

These nuances can not be found in the Guidelines.

#### 4.4 Conclusions

- There is considerable variation in the terminology for describing data and tissue with regards to their 'identifiability'. The Guidelines add to this by introducing a completely new and idiosyncratic typology.
- In the US parlance of 'human subject research' data and tissue which are anonymous on the level of the researcher but contain a codenumber which may connect them to the identifiers of the patient are not considered to be identifiable when the researcher has no access to the key of the coding system. Therefore research with such data or tissue not human subject research.
- The Guidelines that start from this US parlance do not recognise this.
- On the European level the classification of data and tissue matters for the circumstances under which they can be used for research without the consent of the patient, but not for the applicable regime. That is that of data protection legislation. This legislation leaves in some countries considerable room to the use personal patient data for research without the consent of the patient when certain conditions are met. These nuances cannot be found in the Guidelines.

### 5. Ethical review (Guideline 4)

Much can be said about this Guideline. It makes good sense for interventional research but at the same time seems superfluous in that context given that other instruments exist as well, like the general Guidelines.<sup>12</sup>

One would hope that the epidemiological Guideline would differentiate for types of epidemiological research and therefore be different from that of the general Guidelines. However, it does not. It requires the full process of review for any kind of epidemiological research. It also states that the ethical review committee should conduct further reviews as necessary, including the monitoring of the progress of the study.

The commentary to the guideline does not differentiate either. In Europe, many kinds of studies with data do not require ethical review. Ethical review for interventional non invasive studies<sup>13</sup> or quality improvement studies might be necessary<sup>14</sup>, but it is generally accepted that this procedure can be more relaxed and less costly (than e.g. the review of an IND). Instead of ethical overkill the Guidelines could have contributed to cross national epidemiological studies by making such distinctions and clarifying the conditions for the more relaxed procedure or procedures.

<sup>12</sup> And other, like the ICH/GCP Guidance, the European Directive 2001/20, the WMA Declaration and the European Convention on Human Rights and Biomedicine with the Protocol on research.

<sup>13</sup> H. Hearnshaw, Comparison of requirements of research ethics committee in 11 European countries for non-invasive interventional studies, 328 BMJ (2004)p 140-141.

<sup>14</sup> Editorial, Why we need ethical oversight of quality improvement projects, 16, International Quarterly for Quality in Health Care (2004), 343-344.

At odds with present developments is what is being said about multi-centre research. It is stated that each committee should be 'fully empowered to prevent a study which it believes to be unethical'. The European clinical trial Directive has introduced a 'single' review in each country. After that review other committees have lost the authority to prevent the execution of a trial. Such a system existed already in the Netherlands, for all research covered by the Act on research involving human subjects.

#### **6. Guideline 4.1 the need for individual informed consent**

Here again one does not see the usual distinctions. Where the guideline states that informed consent can be waived this refers sometimes to situations which do not constitute human subject research at all according to accepted definitions. In other situations which do not constitute human subject research, the guideline still requires informed consent.

#### **7. Guideline 4.2 informed consent for the use of stored biological samples**

The Guideline requires informed consent which should be specific for the conditions of storage, future access and potential uses.

Much could be said about this subject. Again the Guideline is at odds with national legislation and developments on the national level.

Insofar as consent is required according to other guidelines, etc., there is a trend towards 'broad consent' not specific.<sup>15</sup>

More importantly, nowadays the use of residual tissue for research is considered less exceptional and most legislations (France is a notable exception) do not require informed consent for the use of type 4 or even type 2 of tissue (and of course not for type 3) for research. We have seen this in the US where such tissue been excluded from 'human subject research' by definition. In Europe in 2004 two national legislators (the UK and Denmark) after a balanced and democratic procedure excluded type 4 tissue from the informed consent process. At the same time the German Ethics Council issued a report which proposes the same.

The miscomprehension about this issue can be shown by the statement '....for future epidemiological use of stored biological samples, the investigator (my emphasis) must obtain the voluntary informed consent.....' The point is of course that the investigator, whether an epidemiologist or pathologist etc., does not have a direct contact with the patient and cannot ask such consent. Furthermore the idea is that privacy enhancing technologies will be implemented so that the investigator will not know who the patient is or was either. Hence the use of type 4 data and tissue.

#### **8. Guideline 5: obtaining informed consent: essential information....**

This guideline gives an abundant list of topics about which the prospective participant should be informed.

Again no distinction is made between types of research. Some, if not most, topics are simply not applicable to data research.

If they are not applicable, it should be possible to leave them out of the consent form completely. Not have them in it, but with the addition 'not applicable'. The same holds true if a certain requirement would in principle be applicable but a waiver has been obtained for this specific case, like a requirement for no-fault insurance might be waived in the case of interventional research which involves minimal risk of harm (non-invasive interventional research). Loading the patient information form with this ballast of information which is not necessary to make an informed choice, could lead to serious under representation of the less literate in such research.

<sup>15</sup> B.M. Knoppers, Biobanking: International Norms, 33, Law, Medicine & Ethics, 2005, 7-14.

The Guideline could have helped epidemiological research here by making these distinctions and showing what is necessary to add related to what kind of research. Again, it does not.

Hereinafter I will discuss by way of example some topics, which could be applicable to data and tissue research but which are considered quite differently under at least European legislation than is done in the Guideline.

*No. 7: .....individual subjects will be informed about any finding that relates to their health status*

A complicated subject which is not discussed in the commentary. The issue could arise with research on samples (type 4)<sup>16</sup>.

The general trend is that for several reasons no individual feed-back will be given. Many tissue banking projects, which have been established with patient and carer involvement, do not, as rule, give individual feed-back.

One of the reasons is that tests performed for research are usually not sensitive enough for individual predictions. Another is that the clinical meaning of a new finding might be unclear. Yet another is that, even though it are formally type 4 data, the privacy enhancing technologies used would make it quite difficult to retrieve the individual patient/donor.

My main argument is that anything which is found on the level of the donor, if scientifically valid, will apply to others with the same characteristics as well. It should be generally applied in health care, if effective, and donors will be informed about it via information on the general outcomes of research.

This is not whole story, admittedly. But either one tells it well or one does not. Just like the guideline, I have done neither here. I gave some counter arguments against the sweeping statement in the guideline.

If the guideline would take itself seriously, it would give a balanced view. And it should at least mention that this information cannot be given by the investigator but should be given by the treating physician or general practitioner and will not be given at all if the donor has expressed that he/she does not want this kind of information. Both principles are generally accepted and ignored in the guideline under no. 7.

*No. 8: subjects have a right to access to their data on demand. If not the ethical review committee should have approved of this and this must mentioned in the information*

The European data legislation grants an exception for disclosure on demand in the case of scientific research. This exception has been implemented in most national data protection Acts.

*No. 14: .....when there are different levels of data protection, the information should be explicit about this, explaining the modes of protection at each level in general terms.*

In none of the consent forms for data studies (of whatever type) I have seen this kind of explanations and quite rightfully so. The level of protection should of course be sufficient. If not, the study should not be performed. The prospective participant should not be bothered how this protection is achieved.

Of course, it should be explained how data are gathered and which type of data (or tissue) will be used. If, with type 1 and 2 data, an internal distinction is made between 'contact data' and 'research data' that can be explained as well.

*No 20:.....whether the participant will receive monetary or other benefits from the developments of such products (commercial products developed form biological samples)*

It is generally accepted in Europe that tissue as such should not give rise to financial gain. Which does not imply that this shouldn't be mentioned. However, the message will be different than is suggested by this part of the guideline.

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<sup>16</sup> If the tissue for this research is not residual tissue but taken out specifically for the research, consent would of course be needed. The research would be both interventional and invasive.

**9. Appendix: some remarks about the European regulatory approaches to 'identifiability' of data and data for research (excerpt from a longer article)**

The European Union enacted a Directive on the protection of personal data (95/46/EC). Member-states have implemented this in their national data protection legislation. The Directive names the entity which holds the personal data *and* decides upon their use as the 'controller'. To determine whether data are personal 'account should be taken of means likely reasonably to be used either by the controller or by any other person to identify the data subject' (Recital 26).

On the level of the controller one usually distinguishes between directly and indirectly identifiable data. Directly identifiable data hold direct identifiers, like name, address, etc. of the data subject. Indirectly identifiable do not do so. They are still considered personal data as the *controller* could in principle retrieve the data without excessive means. This is of course a rather subjective criterion. I have described elsewhere instances where no Indirectly identifiable data can be coded, but that does not change their status. They are personal data already by their identifiability by the controller.

Data which are non personal data, so are anonymous data at the level of the controller can be coded as well. They will arrive at the controller, the researcher, with a code which has been transcribed from the direct identifiers of the data subject by the original controller of the data. Here some of the major differences between the legislative solutions of the various European countries start. The majority of the countries hold this category of data which are unidentifiable at the level of the controller but with a code, to be personal data. Other countries, like the Netherlands and the United Kingdom, don't.<sup>17</sup> Hardly ever mentioned in the discussion is the elegant solution of the Austrian data protection Act.<sup>18</sup> This Act distinguishes a category of data which could be identifiable if the controller would use illegal means. A lighter regime applies to these data (par. 4.1). This means a.o. that researchers may use these data without the consent of the data subject, even if they are 'sensitive data', like data pertaining to the health of the data subject, in the sense of the European privacy Directive (par. 46.1)

A study on the implementation of the data protection in the member-states has been published in 2002.<sup>19</sup> The European Commission in its report after this evaluation noted the mentioned difference in interpretation but did not decide upon the question whether data which are anonymous on the level of the controller but are coded, should be considered personal data or not. It did state, however, that the definition in the Directive should be applied with some – in my words – common sense.<sup>20</sup> To my opinion this implies that the Commission is in principle sympathetic towards the view that these data are not personal data or at least should not be treated as personal data.

The European Commission did never 'intervene with a rational and simplified approach' as suggested by Knoppers and Saginar.<sup>9</sup> The report they refer to (in their note 4) was by an ad hoc working group established by the Commission with no legal status which has been dissolved after the luxurious presentation of its report. The distinctions made in this report are at odds with the distinctions made in the data protection Acts as described above. It should further be noted that anonymisation or anonymised has never been recognised as a category separate from anonymous in the regulations which I have examined. Which is logical as it is the result which should count.

<sup>17</sup> Quanthem K. van, Controlling personal data – the case of clinical trials, 8, Privacy and Informatie, 4, 2005, p. 155-161.

<sup>18</sup> Datenschutzgesetz 2000, available at <http://www.bka.gv.at/datenschutz>, last visited august 2005.

<sup>19</sup> The report does not seem to be accessible anymore on the Commission's website, see [http://europa.eu.int/comm/justice\\_home/fsj/privacy/lawreport/index\\_en.htm#firstreport](http://europa.eu.int/comm/justice_home/fsj/privacy/lawreport/index_en.htm#firstreport).

<sup>20</sup> COM (2003) 265 final, available at: [http://europa.eu.int/eur-lex/en/com/rpt/2003/com2003\\_0265en01.pdf](http://europa.eu.int/eur-lex/en/com/rpt/2003/com2003_0265en01.pdf)

The differences in national regulations, which are far more complex than just the status of data which are coded but anonymous on the level of the researcher, result in complications for European biomedical research projects. Privacy enhancing technologies (PETs)<sup>21</sup> which hide the identity of the data subject or even of the treating physician from the researcher, are used in all of these projects but in a different way. In Germany a sophisticated and therefore rather complex system of PETs and a trusted third party has been implemented for all German disease driven research projects.<sup>22</sup> This system complies with the high and because of its federative nature, complex standards of German privacy legislation(s). It could be an example for European projects. However, it presupposes a standing ICT infrastructure which is difficult to attain for projects based on temporary grants. It furthermore presupposes a consensus of what constitutes an acceptable safe system on the European level as has been the case in Germany on the federal level. The danger of this approach could be that researchers of countries with a more moderate system would have to abide to that of the most complex and strict system. A solution could be that the researcher which sends the data in to the central research facility would still be considered the 'controller' of these data. In that case the legislating of the country where this researcher is based would be applicable, not that of the central facility. The central facility would be the mere 'processor' of the data in terms of the European data protection Directive.

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<sup>21</sup>about which e.g. 'Privacy by design, available at:  
[http://www.cbpweb.nl/downloads\\_technologie/Witboek\\_PET.pdf?refer=true&theme=green](http://www.cbpweb.nl/downloads_technologie/Witboek_PET.pdf?refer=true&theme=green)

<sup>22</sup> Reng C.M., et al., Akzeptiertes Datenschutzkonzept, 100, Deutsches Ärzteblatt, 22, 2003, A2134-2137.