Interview

Interview with Prof. Dr. Elmar Doppelfeld on the significance of the Recommendation of the Council of Europe on research on biological materials of human origin: Comments on the WMA Taipei Declaration and legal protection of the rights of a donner of biological material*1

Elmar Doppelfeld　World Medical Journal

Interview:
Chieko Kurihara　National Institute of Radiological Sciences, National Institute for Quantum and Radiological Science and Technology
Takeo Saio*2　Department of Internal Medicine and Psychiatry, Fuji Toranomon Orthopedic Hospital

(Saturday, October 22, 2016, during the WMA General Assembly, Grand Hyatt Taipei, Taiwan)

Rinsho Hyoka（*Clinical Evaluation*）. 2018；46：W21-W28.

*1 This is an interview, during the term of the World Medical Association General Assembly, at its venue, Grand Hyatt Taipei. Japanese translation of this interview is published in *Rinsho Hyoka* (*Clin Eval*). 2018; 46(1): 119-26.

*2 An associate member of the World Medical Association; A member of the Japan Medical Association

1. WMA's Taipei Declaration and the new Recommendation CM/Rec(2016)6 of the Council of Europe

Prof. Dr. Elmar Doppelfeld, during the interview.

Interviewer　In the previous interview with you in 2014[*3], you told us about the issue of broad consent, as the Chairman of the Working Party to elaborate the "Recommendation Rec(2006)4 of the Committee of Ministers to member states on research on biological materials of human origin"[*4]. Now we would like to ask you to introduce the revision of this Recommendation Rec(2006)4 to the new "Recommendation CM/Rec(2016)6 of the Committee of Ministers to member States on research on biological materials of human origin"[*5]. Also we would like to ask for your opinion about the World Medical Association (WMA)'s Declaration on health databases and biobanks[*6].

Doppelfeld　The Working Party to elaborate the "Additional Protocol to the Convention on Human Rights and Biomedicine, concerning biomedical research CETS 195"[*7] included into the draft a specific chapter on research using stored biological material of human origin and related data. All members of the Working Party including me were convinced on the need to regulate this expanding field of research. However in view of the diversity of already existing national regulations with different character some Member States of the Council of Europe did not want to cover this field by a binding legal instrument. So research on stored materials was excluded from the Research Protocol. By decision of the Committee of

---

[*3] Mungherera M, Kloiber O, Doppelfeld E, Kumar A, Jorge MR. Kurihara C, Saio T, interview. The WMA Council Session in Tokyo, 2014: Globalized medical ethics and research ethics – Interview with Dr. Margaret Mungherera, Dr. Otmar Kloiber, Dr. Ajay Kumar, Prof. Dr. Elmar Doppelfeld, Dr. Miguel R. Jorge –. *Rinsho Hyoka* (*Clinical Evaluation*). 2014; 42(2): 553-90. Available from: http://cont.o.oo7.jp/42_2/p553-90eng.pdf

[*4] Council of Europe, Committee of Ministers. Recommendation Rec(2006)4 of the Committee of Ministers to member states on research on biological materials of human origin. Adopted by the Committee of Minister on 15 March 2006 at the 958th meeting of the Minister's Deputies.

[*5] Council of Europe, Committee of Ministers. Recommendation CM/Rec(2016)6 of the Committee of Ministers to member States on research on biological materials of human origin, Adopted by the Committee of Ministers on 11 May 2016 at the 1256th meeting of the Ministers' Deputies. Japanese translation of this document is published in this issue, pp. 127-34.

[*6] World Medical Association. WMA Declaration of Taipei on ethical considerations regarding health databases and biobanks. Adopted by the 53rd WMA General Assembly, Washington, DC, USA, October 2002 and revised by the 67th WMA General Assembly, Taipei, Taiwan, October 2016. Available from: https://www.wma.net/policies-post/wma-declaration-of-taipei-on-ethical-considerations-regarding-health-databases-and-biobanks/

[*7] Council of Europe. Additional Protocol to the Convention on human rights and biomedicine, concerning biomedical research. Strasbourg, 25.I.2005. CETS, No. 195.

Ministers instead of such a protocol a "Recommendation" was elaborated by a new Working Party which I chaired. This version was adopted by the CDBI (Steering Committee on Bioethics) in 2005 during its first reunion under my presidency of this Committee (2005 - 2007).

Later on it was proposed to prepare a revised version of the Recommendation in the light of experience with this text. I became member of the Working Party which presented the actual "Recommendation CM/Rec(2016)6"*5 which was adopted by the Committee of Ministers in May 2016. This revised version is as a Recommendation a legal instrument of the Council of Europe. It is embedded in the Additional Protocol concerning Biomedical Research which itself is embedded in the Oviedo Convention*8 giving the legal frame. The Oviedo Convention and the Research Protocol are legally binding instruments of the international right. The principles laid down in The Oviedo Convention and in the Additional Protocol have to be followed as such and as part of the Recommendation being however itself not a binding instrument.

Interviewer What is the differences between the new Recommendation and World Medical Association (WMA) Policy?

Doppelfeld First, our Recommendation as a legal instrument follows the principles of precision as required for legal instruments. It tries to cover all possible situations. It clearly identifies the kind of tissues addressed and not addressed. Further, it clearly distinguishes the situation between donors who are able and are not to consent to tissue donation including related data. Donors unable to consent are e.g. minors or adults facing different situations leading them not being able to consent in the moment of removal and storage of tissue for research. In the one situation, a person is able to consent and free informed consent has to take place. If a person is not able to consent a substitution of this personal consent by an authorization of a different person or by a body in conformity with national law may be allowed.

In the Recommendation, we have specific regulations for the free informed consent and for its substitution by authorization according to the legal character. Whereas, the World Medical Association (WMA) only speaks broadly on free informed consent. WMA has addressed in the very last moment the situation when tissue is removed from a person unable to consent and on the appropriate procedure when that person gains or regains capacity to consent. This is fine, but nothing is said on the conditions to store this tissues removed from persons not able to consent.

As another difference we can identify is that the Recommendation specifically addresses the ways to get samples for research of course under condition of free informed consent or authorization as pointed out. If a sample is removed for scientific use immediately after the removal the "Research Protocol"*7 applies. In a different situation a person may be asked permission to remove a sample to be stored for future research. This is covered by the Recommendation*5.

In another case samples may have been taken and stored initially only for treatment. These samples cannot be used for research automatically, but in conformity with national law they may be conserved for certain time period as documentation of treatment. We are addressing the case where samples are removed and stored for other purposes than research.

*8 Council of Europe. Convention for the protection of human rights and dignity of the human being with regard to the application of biology and medicine: Convention on human rights and biomedicine. Oviedo, 4.IV.1997. CETS, No. 164.

If a researcher wants to use these specimens for scientific purposes, it is necessary to ask for free informed consent of the donor or for authorization by the legal representative. The same procedure is appropriate if material, initially removed only for a subsequent research project shall we stored for future research. In the WMA document, however, there is no such clear distinction of the situations.

An important issue is the handling of so called leftovers. This problem was one of the reasons for which the Committee of Ministers asked to revise the first version of the Recommendation to bring more precision and clarity. In consequence a specific provision for the use of leftovers was added. It is recommended that in the moment of removal of tissue in any cases the person is asked for consent to use the samples for treatment and for storage for future scientific use. Again, leftovers are by themselves not free for scientific use. The researcher has to be sure that a permission of the person concerned has been given to use the leftover samples for research. If this is not the case, the researcher has to undertake steps to get this permission. If he or she cannot get the consent, research using the materials in discussion is prohibited.

Again, the scope of the Recommendation is broader and the document is more precise than the World Medical Associations paper. In view of precision for instance the Recommendation requires not only an information as such of the donor or of a legal representative. The information shall contain the aims of the research project to preserve the possibility to exclude specific fields of research, such as military research. In addition specific information is appropriate on the right to withdraw consent at any time and the right to ask for removal of the stored material from the collection. Removal is bound mostly to national law.

During the information procedure, the person concerned has to be informed on the consequences of any kind of anonymization of the tissue and of associated data. Furthermore the envisaged donor has to be precisely informed on any kind of prescription to safeguard his or her fundamental right and freedom in that country.

The WMA paper only sticks in this point as in others to the law of the country without introducing specific requirements like the Recommendation does. In the item “Governance” of the WMA paper more or less similar points are listed as in the Recommendation. But in the Recommendation these points are not only listed, specific conditions to fulfill are added. For instance, it is fine to say there should be a procedure on how to deal with incidental findings, but it might be considered as questionable to leave the specific procedure totally to the owner of the biobank.

The owner might say since these are incidental findings, we will not inform the donor. But this would not be acceptable in the line of the Recommendation which underlines the right of the donor to know and not to know. The decision of a donor to refuse any information on incidental findings has to be respected, even in case of findings with consequences for his or her health or for the health of the family?

For the Council of Europe as a lawmaker, it would have been interesting to see which solution the WMA proposes in that situation of incidental findings and even in other positions. These are specific decisions and the WMA paper does not contribute anything to a discussion on these fields in question.

Other points are much clearer addressed in the Council of Europe’s Recommendation. For instance a current information on new scientific events shall be given to the donor or to the legal representatives so that the person concerned may be able to take an informed decision on those evens with the consequence, e.g. to withdraw the consent to use stored

Prof. Dr. Elmar Doppelfeld, during the interview.

material.

From my point of view there are shortages in the World Medical Association's paper concerning the protection of human rights and fundamental freedoms. I had this impression already when WMA presented in Oslo the first version of their draft, asking me personally and also the Committee on Bioethics (DH-BIO) of the Council of Europe to write a comment. I wrote this critical comment which has been totally accepted by the DH-BIO of the Council of Europe. The WMA Working Party which elaborated the new version remarked that Council of Europe had only two points: the question of giving informed consent is not specified enough and the authorization is not clear enough. I wrote a more detailed critical letter to the WMA Working Party regarding these points, there was no reaction from or discussion with this group.

2. Controversy concerning use of material stored in collections

Interviewer There should be controversies among the nations concerning use of stored material.

Doppelfeld There are controversies concerning the use of material stored in collections. In some European countries a donor who has given free and informed consent to store his or her samples for future research will never be contacted again in relation to its use.

The consent is usually given under condition that any scientific use is assessed by an entitled ethics committee and is approved by an authority in conformity with national law. In other European countries – may be in the majority – during the procedure of giving free and informed consent the donor is asked to declare a scope of that consent, which may be restricted to specific research fields.

The donor may express also a general scope "for all kind of research". The donor shall also be asked if he wants to be re-contacted in particular cases or never. In relation to an unlimited scope and to the wish never be re-contacted the donor is assured that tissue will only be used for research projects assessed by an entitle ethics committee and in addition with the approval of an authority if this is required by national law.

If a research project is covered by the given scope there are in this point no problems. However, if a researcher is interested to use a material out-

side the given scope, he or she has to undertake "reasonable efforts" to re-contact the donor to get free and informed consent. It is required by the Recommendation that all steps undertaken to re-contact the donor and failed have to be assessed by the ethics committee. Only when the ethics committee agrees that all reasonable efforts have been carried the samples may be used without re-contact. There are clear conditions for this kind of use outside a given scope and without a free informed consent.

First of all, it must be a research project of scientific importance which cannot be carried out using materials for which consent or authorization is given. There is no evidence that the donor would have refused the envisaged research. I know that these conditions are in conflict with regulations in some European States as pointed out above. To solve this difficulty the Recommendation introduces the procedure to be used "in accordance with national Law".

This point of our discussion clarifies the difficult way to promote scientific research and to protect human rights and fundamental freedom. Hence, most Member States of the Council of Europe require that a person at least should have the opportunity to be asked again and to agree or not to the use of the samples. I assume that the way followed by the World Medical Association is once the sample is given, the ethics committee and an authority decide on the use of that sample.

Also in my opinion, this WMA paper is very late because the problem of storage of material for future research is an old one. As I mentioned in my introductory remarks CDBI of the Council of Europe started to overcome this problem in the mid 90s by a detailed chapter in the draft of the "Research Protocol". However some Member States intervened to prevent a regulation by the "Research Protocol". So, we started in the late 90s to prepare our first version which was unanimously accepted. The reason to revise this Recommendation was the need for more precision and for more clarification concerning e.g. leftovers, dual use of tissues or the detailed governance of biobanks.

Interviewer In Japan, there are two types of uses for stored materials. First type is for biobanking project, which is banking of human tissue with individual identifiable data including genome sequencing data. This needs informed consent where all imaginable future use is explained. Second type, which is widely used in Japan, is asking for consent for future research purpose, not clearly described, but in this case the material is stored and used being de-identified and/or anonymized. In both cases, secondary use research project has to be authorized by an ethics committee.

Doppelfeld We have similar situation in some European Countries. We leave the decision to the ethics committee in conformity with national law. In such case, broad consent may be acceptable to be very broad. If this broad consensus is in conformity with Japanese national law, I have no objections. DH-BIO is not in the position to overrule national law. Law does not mean necessarily legislation; it can be governmental guidelines or regulations.

3. Omitting "biobank" in COE Recommendation paper

Doppelfeld In the new Recommendation the word "biobank" is not used because there is no generally accepted definition of the term "biobank". In our first version, we tried to include "usual collections" and as a separate unity "biobanks". This wording brought a lot of confusion, therefore we omitted "biobank".

One of the approaches to define "biobank" argued, that a typical biobank is a bank which

accepts material for future scientific use, which is in the moment of removal not foreseeable. Researchers may consider a population as interesting, therefore they wish to collect samples for a scientific use in the future not yet identified in the moment of the collection. This type of collection could be addressed as a biobank.

As additional condition the population basis may be discussed, which could be, as discussed, 500.000 people or 1 million. In view of the lack of a clear definition we decided to omit the term "biobanks" and preferred to speak only on "collection of material". Finally we shrunk the wording to "collection of material for scientific use". This wording clarifies that not all collections are addressed, for instance those in a private surgery. By that the Council of Europe clarified that a collection not established for scientific use is not covered by the Recommendation. However, when a physician wants to contribute to research by giving samples of his or her private collection for scientific use, then he or she has to follow our Recommendation. Our Recommendation only includes data associated to tissue and does not cover health database as a whole. After long discussions with data protection specialists of the Council of Europe we restricted ourselves to say "associated data".

4. Reasonable efforts to re-contact

Interviewer In many of the institution in Japan, there are so many secondary use of tissues and data in observational studies, and getting informed consent every time by re-contacting the patient would be burdensome. In such case, we exhibit leaflets or posters in the consulting room, website, or at the hospital entrance, and patients can "opt-out" when they don't want their tissues or data to be used.

Doppelfeld "Reasonable efforts" is a nice word to cover situations where you do not know exactly what is to be done. It is a legal term and which is also used by other institutions like the European Commission. "Reasonable efforts" means the "effort" should be qualified as "reasonable" by an ethics committee. In my opinion, reasonable efforts may be, for instance, to write a letter or to send an email to a person to ask for a different free informed consent, including the wish that the person answers within a given deadline. For instance, in Germany, we are starting a nationwide epidemiological study for the next 30 years with re-contacting the patients. A letter is sent, and if there is no answer, another letter is sent. If there is no answer again, it is tried to contact the person by phone. If this is not possible, it may be assumed that the person agrees to the procedure in discussion.

In some situation where anonymous data will not suffice, the WMA paper requires that the ethics committee express waiver of consent. This is a proposal for a procedure in discussion since the 90s. If it is not possible to get free informed consent for a study, the ethics committee should declare "waiver of consent". This was mostly not accepted, although it is allowed in some countries. "Waiver of consent" is a shrinkage of fundamental rights and freedoms. I do not believe that an ethics committee as such could ever be entitled to take such a fundamental decision. There should be at least a formal legal authorization of the ethics committee to take that decision which is reserved in many countries to courts. So, I proposed to the Working Party of the WMA that the ethics committee may express waiver of consent in conformity with national law. The Working Party of the WMA did not accept this proposal for reasons not known to me.

5. Some other conflicting points

Doppelfeld There are some other conflicting

points. The WMA Declaration only speaks on tissue in collections without any kind of precision of the tissue. I repeat my remarks on the insufficient conditions and on the lack of any provisions for persons unable to consent as donors. It is not sufficient to address tissue of these donors in a collection without asking the conditions for its storage.

I do not think that it is sufficient to listen important points like in the chapter "Governance" of the WMA paper. There should be an additional wording as help for the interpretation of this items. Such an addition would also be helpful for lawmakers to learn the position of WMA. We require in our Recommendation the right of information and its respect. This right is even not mentioned in the WMA paper.

The WMA paper mentions ethics committees without clarifying their position, established on a legal basis or by a private group including medical associations in view of their legal position. Without such a clarification it seems not to be justified to charge ethics committees with responsibilities touching basic human rights. I miss in the WMA paper any provision to prevent stigmatization and discrimination of donors. Of course those provisions are entailed in the Recommendation.

The protection of human tissues transferred to an other country bears known problems. The Recommendation requires for such a transfer that the recipient signs a contract with the donor or with the collection that all protective provisions as given in the country of the donor are respected in the country of the receiver.

In conclusion I think that the Recommendation is a stronger and more precise protective instrument than the WMA's Taipei Declaration.

Interviewer　Thank you for your meaningful insights and scrutiny directed toward further elaboration of newly developed international agreement on ethical consideration of health databases and biobanks. Also appreciate precious introduction of the document of the Council of Europe, for which you contributed so much.

Prof. Dr. Elmar Doppelfeld and interviewers.