

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 —^{*1}

Margaret Mungherera (President, World Medical Association)
Otmar Kloiber (Secretary General, World Medical Association)
Elmar Doppelfeld (World Medical Journal)
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Interview :

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(April 25, 26, 2014, Hotel Nikko Tokyo, Japan)

^{*1} Japanese translation of this interview is published in *Rinsho Hyoka (Clin Eval)*. 2014 ; 42 (2) : 425-57.

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Abstract

This is a record of interviews with Dr. Margaret Mungherera, President, World Medical Association (WMA); Dr. Otmar Kloiber, Secretary General, WMA; Prof. Dr. Elmar Doppelfeld, World Medical Journal; Dr. Ajay Kumar, Indian Medical Association; Dr. Miguel R. Jorge, Brazilian Medical Association, during the 197th World Medical Association (WMA) Council Session held at Hotel Nikko Tokyo, Japan, 24-26, April 2014.

This interview article follows our articles on the Expert Conference held in the spring of 2013 in Tokyo on the draft proposal of 2013 revision of the Declaration of Helsinki (DoH). However, this interview does not only focus on the issue of DoH finalized in October 2013, but also various issues concerning medical ethics, research ethics, which the WMA has been discussing in the era of “global ethics”.

Dr. Mungherera talked about this difficult situation and her initiative to improve medicine and medical research in Africa. Dr. Kloiber talked about some critical points of the finalized DoH as well as fundamental ethical principles. Dr. Prof. Doppelfeld talked mainly on the issue of compensation for research-related injury which is the most influential revision of the DoH. Dr. Kumar talked about the story of Dr. Ketan Desai, who is nominated for future president of the WMA. Dr. Jorge talked about the actual situation of medicine and medical research in Brazil.

We hope this article supports the dissemination of WMA's laudable activities to improve world health in the era of globalization.

Key words

World Medical Association (WMA), Declaration of Helsinki, medical ethics, research ethic, globalization

Rinsho Hyoka (Clinical Evaluation) 2014 ; 42 : 553-90.

I. Interview with Dr. Margaret Mungherera, President, World Medical Association

1. Health in the African region

Interviewer We greatly appreciate that you accept our interview. We learned in this Council Session that the World Medical Association (WMA) is engaged in several activities related to global health and promotion of ethical standards among physicians including the Declaration of Helsinki (DoH)¹⁾. Especially you, as the President of the WMA, discussed very much important initiative of WMA for the health problem of African countries.

Our journal has published a number of interviews and discussions concerning the DoH^{2~11)}, and it is impressive that you coming from a resource constrained country are President in the year of 50th anniversary of the Declaration. We hope that people focus more on the topics of “resource poor settings” and for the global, universal health issue.

Mungherera I also appreciate this opportunity of interview, during the 197th Council Session of the WMA in Tokyo (Photo; Box, page 557). In 1990 the Millennium Development Goals (MDG) were

accepted by the countries in the world. The African countries overwhelmingly approved it but they have largely not been able to meet the goals.

Although globally throughout the world the people are healthier than they were in 1990, in some areas of the world especially in Africa people are less healthy than they were in 1990. Africa comprised 11 percent of the world’s population, but the disease burden in that region is disproportionate to the population. For instance almost 50 percent of the children who die under the age of 5 are in Africa. About 45 percent of the women who die from childbirth-related problems are in Africa. The 67 percent of people in the world with HIV-AIDS are in Africa. And yet it only has 11 percent of the world’s population. The life expectancy at birth in many countries in this region is 40 years of age or less.

The stronger the national medical associations are, the better the health outcomes is. This is because the national medical associations have a role to play in influencing the health systems of their countries. There are several factors respon-



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Dr. Margaret Mungherera, the President of the World Medical Association

Dr. Margaret Mungherera, the president of the World Medical Association (2013-2014) is a Senior Consultant Psychiatrist, Mulago Hospital, Kampala, Uganda. She has been a medical doctor for 30 years and a psychiatrist for 20 years with Forensic Psychiatry as her specific area of interest. She has expertise in training health professionals and Community Health Workers (CHWs), mental health research, human rights advocacy, non-profit organizational governance and development.

Academic Qualifications:

1982 Bachelor of Medicine and Bachelor of Surgery (MBChB), Makerere University Medical School, Kampala, Uganda; 1984 Diploma in Tropical Medicine and Hygiene, London School of Tropical Medicine and Hygiene University of London, UK; 1992 Masters of Medicine (Psychiatry), Makerere University Medical School, Kampala Uganda; 1993 10 week summer program on HIV/AIDS Research methodology, Center for AIDS; Studies (CAPS), University of California San Francisco, USA; 2002 Clinical forensic psychiatry attachment to Keel University Forensic Psychiatry, Department and The Foundation, Stafford.

Source of this profile and further detailed information is in the following web-site:
http://www.wma.net/en/60about/40leaders/CV_Mungherera.pdf

sible for the huge burden of disease in Africa – apart from natural disasters, such as floods, famine, landslides and the weak health systems.

According to the World Health Organization (WHO) a health system is defined as having 4 elements, namely personal healthcare; population health services; national health research; and health in all policies. In personal health care services, governments in Africa have made efforts to provide treatment of diseases. However, there is inadequate attention to prevention of diseases. There is particularly low emphasis on health literacy programs that would equip the population with information regarding causes of illness and how to prevent themselves from getting ill.

Health financing is another challenge in Sub-Saharan African countries. Like in so many other low income countries in the world, between 20-40% funds allocated to health sectors in Africa from

domestic and donor aid, are wasted as a result of corruption or interventions which are not needs based. There is lack of social protection mechanisms need to ensure access to health care without financial hardships. Several African either lack public health insurance schemes or are just piloting them. This has contributed to high costs of basic health care and also contributed to the high morbidities and mortalities in Africa. The high costs of health care has also contributed to millions of people in Africa becoming poorer. As a result, approximately 50% people in Africa live on less than one US dollar a day. This is because people who are ill are not productive, they can not work or save or invest.

2. The WMA African Medical Initiative

Mungherera The difference between countries

with good health outcomes and those with poor health outcomes is the strength of the professional leadership provided by the national medical associations. The influence of national medical associa-

tions in Africa is generally weak. There are even a few countries which do not even have a national medical association. Therefore the WMA will embark on a capacity building program for the

Box

The 197th World Medical Association (WMA) Council Session was held at Hotel Nikko Tokyo, Japan, 24-26, April 2014, co-organized by the WMA and the Japan Medical Association (JMA). The representatives of the national medical associations intensively discussed about the two proposals by the Medical Ethics Committee: statement (on person centered medicine) and declaration (on health databases and biobanks); and 17 statements and other proposals by the Socio-Medical Affairs Committee (health and environment; health care in danger; chemical weapons; violence against women & girls; recruitment of physicians; human reproductive material; reality TV; trafficking with minors and illegal adoptions; aesthetic treatments; physicians' well-being; role of physicians and national medical associations, social determinants of health and health equity; air pollution; solitary confinement; protection of healthcare workers; street children; WMA advocacy). Among these, JMA is going to lead the topics, especially of health database and biobanks; air pollution, etc.. There are also several agendas of the Finance and Planning Committee.

It was also officially announced that the 50th anniversary ceremony of the Declaration of Helsinki is to be held on November 11, 2014 in Helsinki (Finland).

On the last day of this Council Session, April 26, Prime Minister Shinzo Abe visited to give a speech, which all the attendants stood up and welcomed (Photo). The Prime Minister celebrated this meeting where 40 national medical association members have attended and expressed his respect for WMA's 67 years long activities to improve the world standard of medicine and establish medical ethics. He also mentioned that we should keep universal health insurance and free access of Japanese medicine for the next generation and convey the model of long life society to the world. Prime Minister of Japan and His Cabinet. Available from : http://www.kantei.go.jp/jp/96_abe/actions/201404/26ishikai.html



At the previous night session, Norihisa Tamura, Minister of Health, Labour and Welfare also visited and gave a speech to celebrate WMA's activity, mostly focusing on the 50th anniversary of the Declaration of Helsinki (Photo).

Report in Japanese on this Council Session of Japan Medical Association is available from: http://dl.med.or.jp/dl-med/teireikaiken/20140508_2.pdf



national medical associations in Africa. Only 21 of the 54 countries are represented in the WMA. So one strategy will be to encourage those who are not members, to join. Of the 21 who are members, less than 5 are actively participating and are therefore benefiting from the leadership development opportunities of membership.

The planned strategy is to initiate regional forums – a western, eastern, central and southern and northern forum. We shall provide networking opportunities through facilitated online discussions and skills training workshops. We shall also organize a regular African conference, the first scheduled for 3-5 March, 2015.

Another strategy to be used will be to invite strong national medical associations to twin with and therefore mentor African national medical associations. For example, Japan Medical Association has offered to twin with the Malawi Medical Association and the Danish Medical Association will be encouraged to strengthen its twinning with Rwanda Medical Association.

Interviewer In African countries, is the membership of doctors to medical association mandatory?

Mungherera In many African countries, it is voluntary. There are a few countries where membership is mandatory. Even the membership to associations outside Africa such as the American Medical Association and the British Medical Association is voluntary but every physician is represented by either his or her specialty body or college. Membership to the French and German medical societies is mandatory. In Uganda, my home country, we are trying to get a law passed in Parliament that makes membership mandatory. There are a few countries in Africa where mandatory membership is required by law. An example is Tunisia. The advantage of mandatory membership is that you are able to ensure that all physicians

have access to continuing professional Development. In addition, it helps know who is genuine and who is fake. And lobbying for better conditions is more likely to be more effective when the numbers are large.

3. Declaration of Helsinki and capacity development

Interviewer Now, I would like discuss about the post-trial access issue. At the time of finalization of 2013 revision of the Declaration of Helsinki, during the WMA General Assembly in Fortaleza (Photo), during the final process, you proposed to delete two sentences of the provision 20 of the draft version (“If the above conditions are met, consideration may also be given to ensuring that the group receives a fair level of additional benefits. This must be reviewed by a Research Ethics Committee.” These proposed sentences were deleted.). This was because commercialising participation in research in poor countries encourages “dependency syndrome” among the communities who participate in research. In addition, it stifles local research as researchers may not be able to offer the communities or individuals the same level of benefits.

Mungherera That’s what I said, and it has already created a dependency syndrome in Africa. Over the last 30 years or so, there has been a movement in African countries to develop local researchers and therefore strengthen health research. Several African have been trained both within and outside Africa and offer to carry out research in exchange for monetary or other benefits. Often the researchers funded by large pharmaceutical companies will carry out research not because the research is needed but because of the monetary benefits. Then when the local governments or researchers want to do follow up research, the



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communities will refuse to participate even when it is clear that there will be long term benefits in terms of improved health care.

We are trying to make the community, the public, the population to appreciate that research is part and parcel of healthcare and should not be commercialised. Compensation for any injury as a result of the research is acceptable.

Interviewer How is your opinion about the discussion on “reasonable availability” and “fair benefit”? Ezekiel Emanuel, bioethicist in the United States wrote an article with African researchers, published in *Hastings Center Report* ¹²⁾.

Mungherera My argument is that in poor countries, the populations are vulnerable to being unknowingly exploited by those who should be protecting them. This is because the research committees are often not qualified and are not regulated under any legal framework. True, the fair benefits principle is aimed at protecting vulnerable communities from exploitation. But leaving the research committees to determine what is fair in such circumstances does not help achieve that objective.

In Africa right now, many countries lack legal framework for regulating research though the number that has is increasing. In some countries, research ethics committees are made up of people who are not qualified, do not have the independence of mind or the necessary integrity and therefore easily compromised. In my country, Uganda, the National Council of Science and Technology is registering research ethics committees and carrying out training, has made progress but is not yet there.

But the Declaration of Helsinki as it is now will be effective in ensuring protection of the vulnerable communities in poor countries.

4. Declaration of Helsinki and use of placebo

Interviewer And how was your engagement in the discussion about placebo-controlled clinical trial on prevention of mother to child transmission of HIV in African countries?

Mungherera There was a research being done

in the past in Uganda on HIV-AIDS, specifically, the prevention of mother to child transmission. They would start the women on HIV medication and then when they deliver they would stop the medication.

But now, the DoH requires that once pregnant women participating in research are started on ARVs, they must be maintained even when the research ends. So the requirements for post-trial arrangements as provided for in the DoH will be very beneficial for poor communities that participate in research.

I was given the responsibility to go and consult the African national medical associations that had not been able to participate in the regional consultation meeting in South Africa. The national medical associations in countries in South America had raised concerns that showed that they were not agreeable to use of placebo. The general position of the African national medical associations was that the African medical associations generally were of the opinion that placebos can be used if there is no additional serious or irreversible harm.

I think the biggest debate was on whether we should use the “best available option” as control in the clinical trials. The opinion was that that may discourage research. So they agreed to using the “best proven treatment.” There was concern that when pharmaceutical companies use the best available option as a control, the governments which have to continue with the treatments if the research findings recommend its use may find it unaffordable.

So we said – “*Where no proven intervention exists, the use of placebo, or no intervention, is acceptable; or where for compelling and scientifically sound methodological reasons the use of any intervention less effective than the best proven one...*” – so that was acceptable. The use of placebo or no intervention is necessary.

I think we have to keep remembering that this is

not only for pharmaceuticals company-funded clinical trials. This is for other research as well. It is also for locally-funded research. As long as it does not cause additional risk of serious or irreversible harm as a result of not receiving the best proven treatment, as long as those safeguards are put there, there shouldn't be a problem with the use of placebos.

5. Mental health in Africa and in the world

Interviewer So another topic, how is the situation of rational drug use in African countries? We are asking this because in Japan, especially in the area of psychiatry, there is a very serious problem of poly pharmacy: 10 or 20 drugs are prescribed for one patient. And this can be covered by public health insurance.

Mungherera Yes irrational drug use especially poly pharmacy is common. Contributory factors include poor quality of training of health professionals found in several parts of Africa. This we are making some progress in addressing. The other problem is poor access to Continuing Professional Development especially for health workers working in remote areas there is often poor access to the internet.

The other challenges that African countries are trying to overcome are the weak regulatory systems for drugs and health workers.

Universal health access will not be achieved until access to mental health services improves. Unfortunately, in some countries private health schemes discriminate against mentally ill people. We need to train a whole range of mental health workers – social workers, clinical psychologists, occupational therapists. Every single general healthcare worker at the primary level should be able to recognize the common conditions and the health problems and is

able to give some sort of treatment and refer appropriately.

Because of shortage of mental health specialists, our role as psychiatrists in poor countries is to train and supervise unspecialised general health workers working in primary and referral health facilities. Our other important role as psychiatrists, is to carry out research. And another important role for mental health specialists is to carry out advocacy.

We need to get everybody to talk about mental health because it is a cross-cutting issue. You can't get universal health coverage, you can't talk about MDGs, you can't talk about good health outcomes in malaria, in TB, in HIV-AIDS, unless you integrate mental health. So mental health must be integrated in reproductive health services cancer, care, child health care, etc..

The majority of mental health problems can be treated by health workers who are not mental health workers. Psychiatrists should only treat those that require psychiatric drugs which are less than 5% of people who are mentally ill. The rest can be handled by social workers, and counsellors.

We need to carry out strong advocacy at every level for mental health services and it is one of my areas of advocacy during my term as the President of WMA.

Interviewer That is good message from you. How is the situation of hospitalization of psychiatric patients especially schizophrenic patients? In Japan, long-term hospitalization is a very serious problem.

Mungherera Whereas we are trying to de-institutionalize people with severe mental disorders, like schizophrenia for example, we need to develop the community health services. This can only be done if we have the legal framework and in many countries, they don't yet have the legal framework yet. Many countries in the world do not yet have a national mental health law which can be used to mobilize resources and to develop their mental health services. This is why several countries lack community mental health care services and, therefore, health workers tend to want to keep patients in hospitals unnecessarily. Mental Health specialists are campaigning for deinstitutionalisation of mentally ill patients. However, many governments are



too slow on creating a legal framework that would create mental health services in the community. Mental health services in mental hospitals in many low and middle countries are still very inadequate.

There is also need to train health workers on the ethical issues in mental health. They need to understand that mentally ill people have the right to informed consent, right to refuse treatment, rights to get quality healthcare, which has rehabilitation component in it. They have their rights to confidentiality; right to privacy. But many times those rights are violated by health workers themselves. The health workers are sometimes the ones who stigmatize the patients. So we've got to be very careful that our services make sure that health workers fulfil their ethical obligations and that they or no one else violates the rights of mentally ill people.

6. WMA's statement on natural variations of human sexuality

Interviewer On a different topic, it was very surprising that yesterday WMA told us that there was some law in Uganda that is against homosexuality.

Mungherera Yes. We have a law that has come

up in our country that criminalizes homosexuality. However, there are many countries in Africa and all over the world which criminalize homosexuality.

I think a lot of it is motivated by religious perceptions which a few politicians have used to fulfil their political ambitions. Homosexuality is a normal variation of sexual orientation. Some politicians have claimed that there are people coming from the West are recruiting young people as a form of neo-colonialism.

As a result of strong advocacy, WMA was successful in having a provision in the Uganda law requiring health workers to report to the police patients who inform them that they the patients are homosexual extracted.

WMA has adopted the statement on natural variations of human sexuality (adopted by the 64th General Assembly, Fortaleza, Brazil, October 2013)¹³⁾. We assert that homosexuality does not represent a disease, but a natural variation; and condemn all forms of stigmatization, criminalization and discrimination of people based on their sexual orientation.

The Ministries of Health of our countries are trying to come up with a policy which will protect the health workers so they are able to give services



without having to worry about violating the law. But we are trying to talk against the criminalization of homosexuality. We go on national TV to talk against it.

7. Cultural variations and ethics

Interviewer So how do you think about global ethical principles and the principles to be various depending upon each culture?

Mungherera I think there's a cultural aspect to ethics, and I think a lot is to do with the cultural and traditional perceptions. For instance, in many African and Asian cultures, consent for treatment is an issue for the whole family and sometimes for the whole village. Yet our ethical principles as health professionals are that giving an informed consent should only be a right for the individual patient alone. The communities often have disagreements with the health workers over this issue. We as health professionals need to raise the awareness of the communities why the patient should be allowed the right to independently provide the consent to treatment.

In many parts of the world, traditionally children have no role to play in decisions involving their welfare. The same applies to women. There is need to raise the communities' awareness about the rights of women and children.

8. Research for PTSD and other vulnerable populations

Interviewer We suppose that for such vulnerable people or war-related area, strong protection framework is necessary. How is the research for PTSD (Posttraumatic Stress Disorder)?

Mungherera PTSD is a common finding among communities affected by armed conflict. In some populations the prevalence is as high as 40%. Back

in the 80s, there was research carried out in Uganda after the war which reported that PTSD did not exist. However, subsequent research found that research methodology had been questionable. Subsequent research in Uganda has found high magnitude of PTSD as found in other post conflict communities in Africa. However, Africa has a shortage of people qualified to provide the required psychotherapies.

The only treatments available is counselling where the outcome is often not good.

In many African countries, the mental health services are only available in urban areas and yet the majority of the people who need them are in rural areas.

Interviewer We also heard during the Council meeting that there is some unethical research being done on street children.

Mungherera In poor countries, the street children phenomenon is common. It is also found in high income countries too. This is a vulnerable group whose rights need to be protected. Increasingly there are researchers who have been going to poor countries to carry out research on street children. There have been several reports of unethical research among this vulnerable group. As countries develop their research regulatory systems, violation of rights of street children is declining but it still exists in a few places. Street children are not in school and not at home and so their rights can easily be violated. Unethical research has been observed among both foreign and local researchers. Failure to obtain informed consent and not registering research are among the challenges seen in research involving this group of young people. Another is failure to disseminate the findings to the communities where these street children live. Often the children are enticed to participate with small amounts of money.

9. International migrations of physicians

Interviewer We found it also serious and important issue that WMA discussed about the doctors moving from resource poor countries to rich countries.

Mungherera The Brain drain in the health sector in Africa is massive. We have a human resource for health crisis in Africa. In my country, we have 36 million people and there are 5,000 physicians. And more than 95 percent of those doctors are in the urban areas yet more than 95% of the population lives in rural areas. When physicians and other health professionals leave the country they are reluctant to return their home countries. African governments especially in the Sub-Saharan region have generally not done enough to motivate and therefore retain their health workers. The

WMA is discussing the issue of international migration. However, for Africa, internal migration is becoming a bigger challenge. Some governments have tried to retain health workers by forcing them to stay which though it may be a possible solution is a violation of the rights of health workers. So governments have a responsibility to address the issues that push health workers out of their countries. However, the high income countries which are the recipients have a responsibility to desist from luring health workers working in low and middle income countries.

Interviewer Thank you so much for your precious talk. We learned much from your perspective and wish to convey these important message to Japanese and the world health-related communities.

(Interview: April 25, 2014)



II. Interview with Dr. Otmar Kloiber, Secretary-General, World Medical Association

1. Critical points of 2013 revision of the Declaration: Compensation and research registration

Interviewer We really appreciate that you accept our interview, second time following the previous one just after the Expert Conference on Declaration of Helsinki last year in Tokyo¹⁰⁾. We congratulate the efforts of you and Declaration of Helsinki (DoH) workgroup and other members for the 2013 revision of the declaration. Also the revision of EU Clinical Trial Directive was finalized this April, saying that they “repeal” the previous directive¹⁴⁾, for which you struggled not to allow ethics committee provision to be deleted; as well as posing questions concerning broad consent issue.

So now we would like to ask you about the revised Declaration, first of all, on the issue of compensation. Pharmaceutical companies can give monetary compensation for injured patients, without such difficulties. But in some situations, academic researchers cannot provide big amount of monetary compensation but they can only provide free medical care.

Kloiber We believe that patients should participate in research based on altruistic reason. There should be no compensation for participating in clinical trial, but just compensation for losses that occur resulting from the participation. How much that has to be and what is to be compensated is something that has to be decided in the cultural context. If such non-commercial participation cannot be guaranteed then it may be that the research should not be done. These arrangements are some-

thing that the ethics committee has to see beforehand. When it comes to the compensation of damages, the ethics committee may not be satisfied with the offer of treatment only to compensate for the damage, because a person may not be able to work anymore, have no more income, and he or she cannot raise a family, for instance. So in the future an ethics committee may say: If you’re not going to come up with an insurance or any other system to compensate for any possible damage during your research then you cannot do the research.

Interviewer Next question is about the database registration issue. The 2013 version comes to require any kind of clinical research covered by it to be registered to public database. You explained that after the release of public consultation version there were some opinions on it and the working group discussed and agreed to a higher level of protection of research subjects.

Kloiber Some of the regulations on trial registration have been made in the meantime for clinical trials of new drugs but the Declaration of Helsinki is made for all medical research by physicians involving humans. Let us discuss, what is this rule demanding registration is good for? The demand for registration of medical experiments involving humans has an ethical principle behind it, and that is, to avoid harm. Someone’s experiment may not be indicated because somebody else has done it already. Some drug trials may have failed. In order to make such information available, it is necessary that all of them have to be registered. So this follows the principle of “Do No Harm”.



Dr. Otmar Kloiber, Secretary General, World Medical Association

Dr. Otmar Kloiber is currently Secretary General of the World Medical Association. He has been chief executive of the WMA since 2005. Between 1997 and 2005, he served as Deputy Secretary General and Secretary of the German Medical Association (GMA).

He holds an MD (1984) and PhD (1986) from University of Cologne, was a postdoctoral fellow in the Department of Biochemistry at the University of Minnesota, and was a research assistant at the Max Planck Institute for Neurological Research. In 2006, he was awarded an honorary doctorate by the Victor Babes University for Medicine and Pharmaceuticals, Timisoara, Romania. He was appointed Clinical Professor in Health Administration at the Brooks College of Health, University of North Florida from 2009 to 2013.

More detailed profile is in the previous interview in Clinical Evaluation Vol 41 No. 2 (available from: http://homepage3.nifty.com/cont/41_2/p351-72eng.pdf), quoted from the web-site of OECD: <http://www.oecd.org/health/ministerial/worldmedicalassociationotmarkloibersecretarygeneral.htm>

2. Broad consent issue

Interviewer So let's discuss about broad consent. The EU clinical trial directive was "repealed" and in the new Regulation, new statements on broad consent is included¹⁵⁾.

Kloiber There is a reference to the data protection regulation which is now being prepared as well. So the final answer on how to deal with this issue will be in the new European data protection regulations.

There is the idea that persons can give a broad or blanket consent for the secondary use of their data. The first use is covered by an informed consent. The person has understood what the potentials danger of the research is and has agreed. Some people believe that for a secondary use of the research data, a broad consent, where no specific risk is explained is enough, because this is only research on data. No intervention, no drugs applied,

no blood samples taken. However, danger can arise just from the use and analysis of the data itself. Think for instance about genetic research. A person has given informed consent to study his or her genome for the research of high blood pressure. The risk i.e. to be stigmatized is minimal. And now somebody uses the same data on your disposition for let us – and this is fictional – for your disposition on schizophrenia as a secondary use. Some of the subjects may give broad consent, but they may not want research on a disposition for schizophrenia been done research on their material. And such research may not only affect the person, but also it may affect the family members or relatives of the subjects.

In fact: A simple broad consent for secondary use will completely void any informed consent. Therefore the Declaration of Helsinki determines that you have to ask for informed consent also for secondary use, and only if that does not work because it's impossible or impractical, then an eth-

ics committee must take a substitute decision. Our current work on a policy for health databases and biobanks ¹⁶⁾ will offer practical solution for the multiple use of data for different research projects or other uses but it will still aim to protect the individuals.

Interviewer In Japanese regulations broad consent and secondary use of existing material may be allowed but only after obtaining authorization from the ethics committee, for each specific newly proposed research. Additionally, the regulations require that the researcher make the research information available to the public. In case the person who provided the sample or data wants to withdraw their broad consent, the research on that sample should stop. This is to assure the right of withdrawal of the research subject.

Kloiber Yes, that maybe a solution. But there may be also other solutions. We first would like to discuss the options properly and get a consensus about this. But it is certainly necessary to assure the right of the person to withdraw their consent, if it is practically possible. At the end of the nineties the WMA has discussed the “Decode Genetics”-project in Iceland where all people of Iceland should have their genome information collected. We have always thought that there has to be a way of withdrawal of consent for such studies, there has to be an opt-out rule.

Interviewer Some of the bioethicists in the United States are saying that it would be ethically justifiable to explain to the subject that the researcher does not have a plan to stop the research when the subject want to withdraw consent, if this explanation is not saying that they request the subject to waive their right of withdrawal.

Kloiber I think there is a lot of research where you cannot stop it anymore once it has started and data has gone in. But data should not be published in any way that it reflects back to individual

patients in an identifiable manner. If there is something where individual rights would be touched severely, you may have to consider giving up the research. If it is that the individual rights are not being touched and this particular material cannot be extracted anymore from that, then there is no problem. You have the same situation when study is finished and published, the knowledge is out; therefore, any withdrawal would be ineffective.

To make it more complicated: there are different concepts in the various countries about who is the owner of clinical data. In my own country, this is very clear. It is the patient. And his or her self-determination is an unalienable right. In many of our constitutions the self-determination is being seen as a very high right, it is part of your autonomy. You cannot sell it, even if you wish to give it up, you cannot; not for any price.

3. Living will and human right

Interviewer So similar but a different topic. In Japan when researcher conduct brain imaging study to compare imaging data during living time and brain tissue analysis data after the death of the research subjects, some of the researchers hesitate to explain to elderly research subjects about their intention to conduct brain tissue research after the death of the subjects. Not all the researchers hesitate, but some of them feel it not appropriate.

Of course it is legally required to acquire consent of family after the death of the subject but at the time of involving them in imaging study, it is not legal rules to require them to explain about their intention of research after their death.

Here in Japan, even if the patient or the subject has already given the informed consent for the harvesting of their brain tissue, after the death of that patient, the family still has to give authorization on the use of that brain tissue. How it is in Germany?

Kloiber That would be handled the same way. The family would have to give consent. There are other countries where it is believed that the body of a diseased person is not in the ownership of anybody; that it can be used. Ideally everybody should have a living will that says, what are his or her preferences what it is that the persons want or not, and this should be respected whenever possible. All of these models exist because they reflect the moral beliefs of societies and often religious beliefs.

Interviewer I think that in European countries, there's no consensus that people can define "living will" about what is happening after the death of them.

Kloiber That's correct the rules are different from country to country but I think that in all of the European countries, if you say during your time of life – yes, I agree to such a research use of my tissue for instance – then this is binding. This cannot be overruled by your relatives. The relatives of the deceased person have to respect their will. At least in theory it should be that in all of our countries a person's written consent to donate tissues or organs for research, or for transplantation should be respected. However, to enforce such a

rule "at any price" maybe highly insensitive. Not respecting the will of relatives may not only hurt their emotions, but it may lead to a growing criticism of research or organ donation.

Interviewer Another point, how do you think that some researchers think that it is not good to explain to the elderly person, who is close to dying, that we plan to conduct brain tissue research after their death. Researchers is willing to give the elderly patient clear explanation about the imaging study during the living time of the subjects, but some of them feel it is not good thing to talk about the detailed plan to do brain tissue research after the elderly person's death. In any case, the final authorization would come from the family, so that this elderly person is not the person who will make the final decision on that matter. How do you think about this kind of idea that the researchers will only give very brief explanation because of some "ethical" consideration?

Kloiber The matter here is the discomfort of the researcher. I'm sorry that is not an argument. I don't accept that there is a problem with the elderly persons. I think elderly persons usually well know when time has come that they will die, and actually



for them it is rather less a problem to discuss this, and the discussion has only to go that far as it is relating to their self-determination and dignity. The question of informing about risks when doing research on tissue after death is necessary – think about genetic research and the relevance for the family – but it does not play the role as it does when life continues. The level and extend of information certainly is very different. But again it is a matter of dignity. Lying – even when done by omission – should not be a method for researchers.

My answer to the researcher in most cases would be: if you are not able to explain your research to the elderly person don't do the research. The situation is certainly more complicated when dementia has started or a major depression exists.

Interviewer So in your country, researchers who conduct this kind of research can clearly provide the information?

Kloiber It's not a question of whether they can or want; they have to. In case the person is demented you have to discuss this with the legal guardian or representative of that person as well. But old persons don't lose their rights. Personally, I don't see that this is an unsurmountable problem. I've spoken to many elderly persons, and they are often very willing to help research.

Interviewer That will be the difference between Japan and other countries because in Japan there is no legal rule that establishes informed consent. Ethically it is a matter of course that people have a right to provide informed consent when taking part in research. But at this moment in Japan there is no such kind of legal rule.

Kloiber Well, the self-determination is seen as a human right, and I'm not sure that human rights aren't valid in Japan. So even if there is no specific legislation in Japan I think those rights have to be honored as well.

Interviewer This kind of right, human right, is



assured by the constitution. But in Japan, “freedom of research” is sometimes stronger than human right of research subject. In Japan's constitution there is some provision saying that there is freedom of study. We think clinical research is completely different from purely academic study. This kind of discussion is very difficult.

Kloiber (Long laughter) In many of our legal systems the concept of the freedom of research in science is a derivative of the freedom of speech. And it is a very high right. In my own country, in Germany, for instance, the freedom of research and teaching is a constitutional right –. But that does not mean that you can do whatever experiment you want to do. This freedom – and all freedoms – have their limit where they are in conflict with the rights of others. Here it's clearly the right to self-determination and dignity. I think there is a very clear boundary for the freedom of research.



4. Clinical trial regulations and low-intervention trial

Interviewer Of course in Japan there is a consensus that there is a limit in doing research. But the range of that limit is very narrow. How do you think about the randomized controlled clinical trial using authorized drug in the range of the label? Under the new Regulation in EU (repealing the Directive), this is categorized as a “low-intervention clinical trial”, although it is in the scope of the Regulation.

Kloiber We are not very happy with that regulation because we think it’s very cloudy and not clear. In the Declaration of Helsinki, we do not accept different classifications. The question here is, is the data identifiable, can it lead to a person; shall say: can it do harm; then the Declaration has to be followed.

Interviewer In Japan there is big pharmaceutical scandal involving five universities which conducted 5 different large-sized clinical trials using valsartan. The trials used different protocols but all were within the range of the authorized label

information. It was alleged that there was some fraud. So many people discuss about developing new law to regulate clinical research. But it is very difficult many of the legal scholar say it is difficult to cover legal rules for “low risk” clinical research, because of the reason of “freedom of study” in the constitution.

Kloiber I don’t know what the details of that fraud are. But if you call it fraud, it is obvious that criminal laws have been violated, so that is usually not what we as WMA deal with as an ethical problem or dilemma. When it comes to fraud it means somebody has falsified something in order to have an economic or other benefit from that. That is certainly something that the criminal system has to deal with. But I cannot speak about that case, because I don’t know the circumstances.

Interviewer The Japanese Ministry of Health criminally accused the company. At this moment, the police are still investigating the matter and the result of their investigation is not known yet ¹⁷⁾. But anyway, people are very much interested on how we should regulate clinical trial.

Kloiber In European countries, in the beginning the regulation was only for the marketing authori-

zation. Now it covers also Phase IV studies.

5. Post-trial access and fair benefit

Interviewer Just a short question about the post-trial access issue of the Declaration of Helsinki. At the final moment of the adoption of the 2013 revision, Dr. Margaret Mungherera proposed to delete two sentences of the provision 20: “If the above conditions are met, consideration may also be given to ensuring that the group receives a fair level of additional benefits. This must be reviewed by a Research Ethics Committee.”

Kloiber Not only at the final moment. She was speaking against that kind of idea from the very beginning. She and other colleagues from Africa thought this may be an incentive for groups to ask for payment.

Interviewer There’s also this discussion about “fair benefit”, proposed in an article in *Hastings Center Report*¹²⁾.

Kloiber This is certainly a very well meant idea about how to deal with problems of poor communities. And as you saw in our draft the work

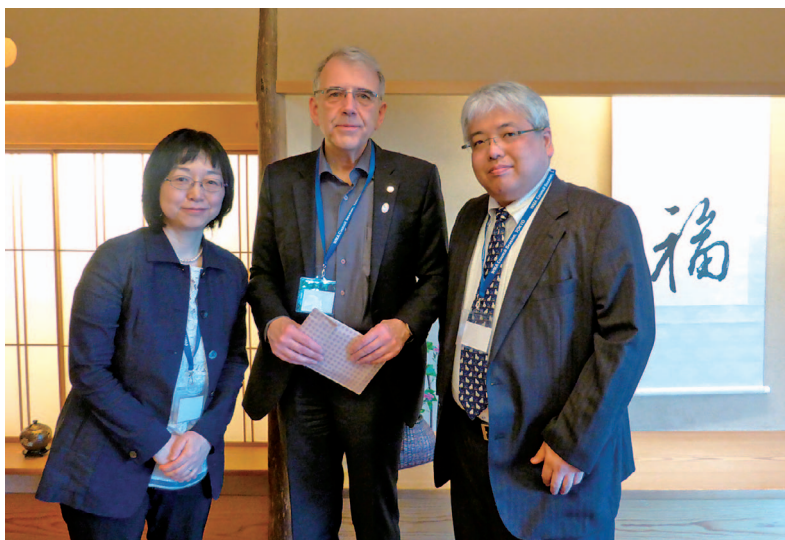
group shared that protective or paternalistic idea. But now our colleagues from Africa come and say, “no, we don’t want that”.

There always has been the idea that if a community participates in research there is additional benefit. Be it a better instrumentation, better staffing, more education for the health professionals, better payments and with that a higher incentive to stay at their places. So I don’t disagree with the idea that there can be an additional benefit or a negotiated benefit. But then our colleagues from Africa told us, no, don’t put this in because some people will come and ask for money first. Therefore this explicit mentioning of additional benefits has not seen as being helpful.

Interviewer Thank you so much, it is very much important information for Japanese research community, as we are going to expand our research more globally, to be able to contribute more to global health. We really appreciate your contribution to this second time interview.

Kloiber Thank you very much for this interview.

(Interview: April 25, 2014)



Ⅲ. Interview with Prof. Dr. Elmar Doppelfeld, World Medical Journal

1. Insurance for research-related harm in European Union

Interviewer It is very nice to see you again, your presentation in the Expert Conference meeting on the revision of the Declaration of Helsinki in Tokyo in the spring of 2013 was very important as it explains the perspectives of Council of Europe^{9, 18)} on the issue of compensation for research-related injury.

Doppelfeld Insurance for research-related harm is required by the Declaration of Helsinki. However the Declaration of Helsinki is not legally binding. Its demand to have such an insurance is an advice. A very good advice, of course. However, the regulations of insurance for research related harms are different from State to State. The Oviedo Convention¹⁹⁾ and the additional protocol to it concerning biomedical research²⁰⁾, only say that there should be an insurance in conformity with national law. In Germany, there is only an obligation to cover drug trials by an insurance. For all other projects of biomedical research on man, RECs (Research Ethics Committees) advise such an insurance, but no researcher can be forced to follow this advice.

Interviewer So in the EU clinical trial directive²¹⁾, there is a description that researcher or sponsor should provide indemnity or compensation. Compensation means that if there is no fault, the sponsor should nevertheless provide the compensation.

Doppelfeld It is the same in my country. The German legislation, the relevant Federal Drug Law, requires an insurance track covering those cases for which in case of damage no other insurance can be taken. It is the duty of the sponsor to

fulfill this legal obligation.

Interviewer The EU clinical trials was “repealed” by the new Regulation and it seems to strengthen the obligation of compensation¹⁴⁾. Is there any specific guideline by government to define the contents and procedure of compensation?

Doppelfeld The actual Federal Drug Law requires 500,000 € per person in case of death or everlasting impossibility to work. All the other points like risk calculation are not done by the government. The insurance companies propose guidelines and regulations (“conditions of insurance”) which have to be permitted by a Federal Authority. The application of these conditions is supervised. The risk calculation in a specific research project may be performed by the company and the sponsor and then be assessed by the legally competent REC. In a case given, a harmed person may go to a court which decides on the compensation to be paid.

Interviewer In Japan there is a drug company’s guidelines for compensation for clinical trial-related injuries, which was developed referring the governmental scheme of remedy for injury caused by marketed drugs. This guidelines define the amount of compensation for death or disability, and also the amount of the payment for medical cost. This is because in Japan approximately 30% of the medical cost is co-pay by the patients, so sponsor will pay this co-pay part for treatment of trial-related injury.

In many of European countries most of treatment is free for patients, so I suppose that this kind of reimbursement of co-pay expenditure is not regarded “compensation for trial-related injury”.

Doppelfeld Right, it is not regarded as compensation. In Germany medical routine care is paid



Prof. Dr. Elmar Doppelfeld, World Medical Journal

Actually Prof. Doppelfeld is member of the board (“bureau”) of the DH-Bio/CDBI. Prof.

Doppelfeld published scientific articles in his original academic field (nuclear medicine) and in an increasing number on ethics in biomedical research.

Dr. Elmar Doppelfeld, physician by education, Professor of Nuclear Medicine at the University of Bonn, was 1982-1994 Secretary General, 1994-2012 Chairman, and is since 2012 Honorary Chairman of the “Permanent Working Party of Research Ethics Committees (RECs) in Germany”, the independent representation of German RECs, the partner of governments, parliaments and public.

In 1992, Prof. Doppelfeld was appointed by the German Federal Government as a member of the German delegation to the Council of Europe’s “Steering Committee on Bioethics (CDBI)”. Prof. Doppelfeld was involved in the elaboration of the Oviedo Convention and was one of the leading co-authors of the “Additional Protocol to the Convention on human rights and biomedicine, concerning biomedical research”. He has been chairman of the working parties which elaborated the “Recommendation Rec (2006) 4 of the Committee of Ministers to member states on research on biological materials of human origin” and the “Guide for Research Ethics Committee members”. He served the CDBI as vice-chairman (2003-2005) and as chairman (2005 -2007).

by the health care system using well established and proven methods. If a person goes to a hospital, he or she has nothing to pay, with the exception to pay 10 € per day during 28 days of stay in a hospital per year. The treatment in the hospital includes drugs during the stay. Drugs in the outpatient department or in a private surgery, are paid with some very low additional costs for the person concerned. If patients in a university hospital are included in a clinical drug trial or in an other clinical trial 80% of the hospital costs are paid by the health care system, 20% by the sponsor of that trial, drug company or e.g. a research foundation. The insurance for routine health care generally does not cover research projects on man unless the company agrees to do so. Again: in Germany only for drug research an insurance is compulsory.

Interviewer So the German people don’t regard

such kind of providing free medical care is not regarded as compensation for the harm.

Doppelfeld No. Of course it is very often discussed who should pay for the treatment for research-related injuries – the whole population or the sponsor? This discussion is still open.

Interviewer And is there any statistical data on the number of cases of the compensation for research related injury? No such kind of statistics?

Doppelfeld We do not know it for insurance companies do not open their books.

2. Investigator-initiated clinical trial and compensation

Interviewer In Japan there are some statistics of the number of the cases of the compensation, for

the case of drug company clinical trial aiming at new drug application²²⁾. However, there are no such kind of statistical data of investigator-initiated clinical research. Through informal conversations, we have not heard about the case of compensation in investigator-initiated clinical research.

And do you know personally is there any cases of providing compensation for the research-related injury in academic research?

Doppelfeld No, not to my knowledge. I cannot exclude it. However, I don't know.

Interviewer Japanese companies are rather willing to pay. But Japanese researcher cannot pay so easily. And another point is that Japanese doctor-researcher conducts "low-risk" research using already authorized drug, sometimes randomized ones. And another aspect is that many of the academic-oriented research is for the very serious, life-threatening disease. In these cases, doctors cannot identify some death or severe damage is because of the research or because of the natural history of that disease. So that is the reason why they don't identify the harm resulting from research.

Doppelfeld In Germany, if you conduct double-blind study, comparing licensed drugs, or licensed drug and unauthorized drug, it has to be covered by an insurance.

In Germany, at least also in the European Union, no exemption of academic drug research is given. The directive says all kinds of research in the scope of the directive have to be covered by an insurance. But after 10 years discussion with our government, we finally got a solution that certain types of drug research with very low risk may be exempted from the obligation to be covered by an insurance. However, the low risk is proposed, but definitively not assessed by the researcher or by the sponsor. The competent Federal Authority and the competent local research ethics committee are responsible for this assessment whether they may

agree or not to the proposal of the sponsor.

3. "Repeal" of the EU Clinical Trial Directive

Interviewer So in the revision of EU Clinical Trial Directive, there was a categorization of "low-intervention clinical trial".

Doppelfeld My last remark addressed the legislation in Germany. The EU Directive 2001/20/EC on clinical drug trials will be repealed by a EU Regulation¹⁴⁾. This Regulation of the European Parliament and of the Council of 16 of April 2014, entering into force in 2016, includes provisions concerning low risk projects.

Interviewer Another important point of the revision of the directive is that some of the clinical trial data is open to public, in EU database, same as US FDA's new regulations.

Doppelfeld The openness of data is a step forward. The German legislator introduced a provision in the drug law that the Federal Drug Authority is obliged to inform the competent research ethics committee, which has actually no access to the EudraCT Database, on data which are of relevance for the safety of research participants. May be that the openness of data will be enhanced by the new EU Regulation.

Interviewer When I saw the first proposal for the revision, I supposed the original intention was to conduct a multinational clinical trial with one ethics committee's authorization.

Doppelfeld Yes. The hope of pharmaceutical companies is that within Europe, at least within the European Union, there is only one authority to permit a drug research project and only one ethics committee to give the favourable opinion on it. And for that reason the EU-Commission as the author of the new regulation introduced¹⁴⁾ the term "reporting Member State" and charging it with the

definitive decision. It is not bad to have a single portal for the application. However, it is not acceptable to leave this important ethical decision to one Member State by hindering other States to refuse or forbid a project on their territory for ethical reasons. Ethics committees in all States in which a clinical drug trial is carried out, should be involved in the assessment. This is possible within the given time table also in States with a federal structure. In Germany, for constitutional reasons, RECs are part of the administration of the 16 States which constitute the Federal Republic of Germany. This system works! We are, even the pharmaceutical companies, happy with this solution improving the protection of research participants on a legal basis.

4. Ethics Committees in Germany

Interviewer Is there any system of qualification of ethics committee in Germany?

Doppelfeld Yes and not. Research ethics committees in Germany do their work on a legal base, given by the State law. We have 16 states and 16 legislations in Germany. In all State RECs shall be multidisciplinary, some legislations require a pharmacist as a member, some legislations require

patients representatives as members. It is only said, that members “should be qualified”, nothing more in the laws on this issue. In Germany exist 53 RECs. They are established by Universities (the majority), by Medical Associations in the States (not on a federal level) and in three States by their government. They are equal in their rights and their responsibilities. The medical associations do not like this equal position but the legislators decided it, Powerful research institutions in my country insist on their independence, and RECs are a part of this independence.

Members of a REC are appointed by the Medical Association in a State or by the University or by its Faculty of Medicine. We are very often asked by the parliament or by the government to declare provisions concerning the qualification and the continued education of REC members.

We – “The Permanent Working Party of Research Ethics Committees in the Federal Republic of Germany Inc.” – have instituted since 1983 annual, and since about 6 or 7 years semi-annual scientific meetings for the continued education of REC members. More over all RECs offer new members an introductory seminar to prepare them for the new task. The content of these seminars respects the knowledge of the new members. The German sys-





tem of research ethics committees was under question when the EU Directive entered into force in 2004. Pharmaceutical companies proposed to replace it by a system: “One Research Ethics Committee for Germany”. Also in the “Deutscher Bundestag”, our Federal Parliament, a group of politicians was in favour of this solution: “Only one REC”. The “Permanent Working Party” opposed. The Medical Associations underlined, that such a solution would not be in conformity with the Code of Deontology, which is by States decision legally binding in the States. Our Second Chamber, the “Deutscher Bundesrat”, representation of the States, discussed a change of the codes of deontology in the States to allow the system of “One REC for Germany”.

Finally the Deutscher Bundestag decided in the year 2004 during the course of the implementation of the EU Directive to keep the system of RECs. It was recognised that the system has grown up from the bottom to the top and that it works rather well. However the parliament charged the government to

present after 3 years a report on the experience with that system under the new conditions as given by the Directive. This report after 3 years experience stated that unanimously researchers, pharmaceutical companies and authorities did not want to change that system, which is still working.

5. Broad consent issue

Interviewer So ethics committee is a very important topic that WMA make some opinion to the change in EU Directive. Another point is “broad consent”. The WMA’s policy is “informed consent” and they don’t regard that broad consent is ethically acceptable; and also they are discussing about proposed statement on health database and biobanking¹⁶⁾.

Doppelfeld When we prepared in the CDBI (Steering Committee on Bioethics) of the Council of Europe the “Recommendation Rec(2006)4 of the Committee of Ministers to member states on research on biological materials of human origin”²³⁾ we have been aware of the different positions concerning broad or open consent. We kept in mind, that it is accepted since more than 200 years that the protection of human rights and fundamental freedoms is an obligation of the States. Of course it is welcomed that groups like physicians contribute to that protection. But the conditions, the frame of that protection is given by a State in relation to the democratic will of its population. Groups like e.g. physicians cannot introduce regulations binding other groups, e.g. nonmedical researchers using stored biological material of human origin. We knew the position of the WMA and of national Medical Associations. We however decided to introduce the open consent in the recommendation. We got the consent also of governments from countries in which the Medical Associations opposed.

I emphasize that broad or open consent does not

mean blanket consent. I think that the autonomy of a person concerned to agree to take a sample for research includes also the autonomy of that person to decide on storage and further use of the sample. To protect this autonomy and to prevent misuse we introduced specific conditions for the use of stored biological material. First of all, if the envisaged scientific use is in the scope as agreed by the person concerned, no problems occur. If the person has declared his or her wish to be recontacted before use even in this case, reasonable efforts are to be undertaken to recontact that person. If the planned scientific use is not in the scope agreed by the donor, the researcher has to do his very best to recontact the donor, which may be very difficult or even impossible. The researcher has to present to the research ethics committee his efforts to recontact the donor. The REC decides whether this efforts are “reasonable”, e.g. appropriate. If recontacting is impossible, a research ethics committee may give a favourable opinion and, if required by national law, an authority may give the permission to carry out the project under 3 conditions: the research project is of high quality; there is no possibility to perform that research project with material for which a consent is given and no objection of the person concerned is known. I think that these conditions bring a balance between the protection of the individual’s autonomy and the justified intentions of research. Again: the Council of Europe does not favorise a blanket consent.

6. Living will and human right

Interviewer So similar but a different topic. In Japan when you conduct brain imaging study to compare imaging data during living time and brain tissue after the death of the research subjects, some of the researcher hesitate to explain to elderly research subject about their intention to

conduct brain tissue research after the death of this subjects. Especially in such case that this research subject may die in future within 3 or 5 years.

Of course it is required to acquire consent of family after the death of the subject but at the time of involving them in imaging study during their living time, it is not legal rules to require them to explain about their intention of research after their death.

Doppelfeld It is normally understood that the information to seek consent should be full and broad enough that the person concerned may be in a position to decide: to refuse or to consent.

And in my opinion to exclude the intention that after the death of the person concerned a sample from the brain will be taken would be not a valid information; and if the information is not valid, the free informed consent as such is not valid. To intervene in the corpse is a major affair also under ethical considerations and I think that the person should be informed. In addition: I do not think that in Germany the family is entitled to give the consent to use the material of the deceased family member.

Interviewer In Japan there is some feeling that it is not good thing to talk about the situation after the death to the elderly people.

Doppelfeld I know that but you have to respect the person. If you follow the system of free and informed consent as a basic ethical pre-condition then you have to inform fully.

7. Academic research and human rights

Interviewer Just a little bit more question. I heard that in Germany many of the people come to think that investigator-initiated clinical trial to compare two marketed drugs should be funded by

two pharmaceutical companies of both compared drugs, not funded by one. Because if one company funds such trial to compare their drug to another company's drug, the results should be biased.

Doppelfeld The problem exists, but the meaning of the people you mentioned is unknown to me. The study protocol and the financing of the project is assessed by the competent REC and in case of a drug research by the competent Federal Authority. The sponsor and the researcher have to sign a contract which is presented to the REC and to the institution in which the researcher wants to carry out his project, e.g. an university hospital. The sponsor pays the money not to the researcher but to a specific division in the administration of the university. We think that these steps should prevent bias of results. The problem of bias of publication of results certainly is not solved by these procedure. Of course it is not only a German problem that pharmaceutical companies try to sponsor research in universities and to avoid that those trials are recognised as sponsored trials. Some projects start as researcher-initiated trials, and when favourable data have been achieved and collected,

these data may be used as basis for the licensing a specific product of a specific company.

Interviewer Very similar situation in Japan. In Japan there is big pharmaceutical scandal involving five universities which conducted 5 different large-sized clinical trials using valsartan, different protocols but all were within the range of the authorized label information. It was alleged that there was some fraud¹⁷⁾. So many people discuss about developing new law to regulate clinical research. But it is very difficult many of the legal scholar say it is difficult to cover legal rules for “low risk” clinical research, because of the reason of “freedom of study” in the constitution.

Doppelfeld (Laughing) I am not sure about what is happening in Japan, as for the clinical trial scandal. But in Germany, human rights of research participants prevail the “freedom of study”. There is no doubt that there is a limitation to such freedom of the researcher.

Interviewer So thank you very much for your precious talk.

(Interview: April 25, 2014)



IV. Interview with Dr. Ajay Kumar, Indian Medical Association

1. The story of Dr. Ketan Desai

Interviewer Thank you so much for you to accept our interview today. Your presentation of the last year's Expert Conference on the revision of the Declaration of Helsinki was very impressive^{9, 24)}. Our last year's interview with Dr. Otmar Kloiber¹⁰⁾ was also focusing importance to avoid exploitation of vulnerable population in clinical trials.

Also, we are interested in the topic discussed in the Council session that the suspension of inauguration of Dr. Ketan Desai to be the president of the World Medical Association (WMA) is going to be lifted²⁵⁾. Previously, we read an article in the *World Medical Journal* to inform that Dr. Desai was elected as the president but it was suspended because he was accused of the suspicion of bribery taking. However, now we heard that it was found that he is not criminal. So, we would like to ask you to introduce this story.

Kumar Dr. Ketan Desai is a very powerful personality in the medical world of India. Of the 200,000 members of Indian Medical Association, he's the undisputed leader. Also, he was the president of the Medical Council of India (MCI) that looks after the medical education of the country, controlling about 400 medical colleges in India. MCI also regulates the medical practice in India.

On one side, he was the supremo of Indian Medical Association, which is a very powerful body of doctors, and on the other side he was the president of the MCI. Automatically, he became too powerful for the government. Any government would not like such a powerful person in Medical

profession. MCI is a recommending body for starting new medical colleges, giving recognition to the medical colleges and recognition to the post-graduate course in medicine. In India, more than 50 percent are private medical colleges. Some of the politicians either run those colleges or support them, or seek for the admission of their kith and kin to medical colleges. Automatically they have vested interest in the MCI. Dr. Desai was not able to oblige them against the norms of MCI. The MCI was recommending whatever was right after inspecting the colleges.

Sometimes the government went against the advice of the MCI, and gave permission to run the medical colleges. In 2002, the Central Bureau of Investigation (CBI) of India investigated against Dr. Desai for alleged corruption. But ultimately CBI could not find anything wrong. The supreme court accepted the report of CBI giving clean chit to Dr. Desai. The Income Tax department did not find any disproportionate asset of Dr. Desai. He was again elected president of MCI with overwhelming majority.

Second time, the government alleged that Dr. Desai was taking bribe through somebody else from a new medical college for influencing the decisions by MCI. He was arrested by CBI and there was a wide publicity in the electronic and print media nationally and internationally. All the scandalous rumors were spread by those who were disgruntled. They even published that 500 kilos of gold and 500 million Rupees was found by CBI on search of his house. This was all proved wrong in subsequent investigation of CBI.

The government filed cases against Dr. Desai in different parts of the country; located in different



Dr. Ajay Kumar, Indian Medical Association

Dr. Kumar provided world class services to the poor & down trodden while conducting researches in different fields of Urology, results of which were presented, debated and appreciated at various National and international fora.

Source: http://www.mciindia.org/Council_members/CV-Dr.Ajay.Kumar.pdf

corners on fabricated charges. The cases were filed in Delhi, Lucknow (North Central part), Kolkatta (Eastern part), Hyderabad and Chennai the southern part of country.

The CBI started with allegation that he had amassed 300% of extra wealth to his known source of income which was their allegation without substantiation. After 3 years of investigation, they submitted in the court that Dr. Desai had no disproportionate asset. So they prayed to the court, to allow them to withdraw the case of disproportionate asset which the court allowed. The disproportionate assets case was the mother of all the cases which was dropped by the court.

Cases in Chennai, Kolkatta and Hyderabad were dropped. In the case at Lucknow the CBI filed a counter affidavit in the court saying that they have not found any relationship of Dr. Desai with other

MBBS,FRCS(Edin.),FIAMS(Uro),FICS(Uro). Lifetime Service Award during IMACON 2011; B C Roy National Awardee 2007; Urology Gold Medal 2010. President, Urological Society of India (2008-2009); President, Indian Medical Association (2007-2008); Vice President, Commonwealth Medical Association (2007-2010); Member, Council of World Medical Association (Since 2006); Member & Advisor to President, Medical Council of India (Since 2013); Advisor : Confederation of Medical Associations in Asia & Oceania (CIMMAO); Member, Adhoc Committee Indian Red Cross Society, Bihar State Branch.

Practising since 1984 and established Urology as a separate speciality in state of Bihar. After having obtained a degree in medicine from Patna Medical College (formally 'Prince of Wales Medical College') under Patna University, he sailed to England to specialize in the area of urology. He could have very well stayed back to pursue a highly lucrative career there but driven by the sweet smell of Bihar soil, he returned to serve one of the BIMARU (ailing) states, his homeland with enthusiasm. At Patna,

accused persons in the case. Now there is only one case that was in Delhi, the one which was the initial case for which he was arrested. You can understand that on one hand he was arrested being accused of amassing disproportionate asset and on the other hand CBI itself said that they have not found anything on his possession – either on the body or in his office or in his house which was disproportionate to his income. The Supreme Court stayed the proceedings in this case in the lower court at Delhi.

After arrest of Dr. Desai, the Government of India superseded the MCI by an Ordinance. The superseded MCI being an autonomous body has representatives from state governments, medical universities, medical graduates of different states and 8 nominees of central government. The central government then appointed 6 handpicked medical

professionals to run the organization which was earlier being run by about 100 members elected or nominated from all over the country. The motive of the government was clear that they wanted to demolish the autonomy of a regulatory body to run it in an autocratic way through their 6 nominated people who hardly had any experience in running such organization. After the supersession of MCI medical fraternity started protesting vehemently. The whole medical community was up in arms. The parliament of India took notice of this. The parliamentary committee on health which consist of member from all the political parties in the parliament, after extensive investigation, reported to the parliament that the government did not take the right step to supersede MCI, which is an autonomous body and suggested to restore it as soon as possible.

The parliament accepted the report and directed the government to reconstitutes the MCI according to the Act of 1956. The MCI was reconstituted in

December 2013 according to the Act and representatives from different sectors were either elected or nominated.

Interviewer We regard it very much important story that Indian medical professionals struggled to keep their autonomy. Is there any personal conflict with any other person? We suppose that governmental, political issue may be stronger than personal conflict.

Kumar Well, he had some personal conflict with some powerful lobbies in the government. As I told you, he could not extend the undue favour to them which they wanted.

One doctor, based in US and not living in India, after the arrest of Dr. Desai, started a canard against him. He kept on writing about Dr. Desai, falsely accusing him in different matter and passing his own judgment. He filled cases against Dr. Desai in different parts of India including supreme court and he lost all the cases. As a matter of fact, in Gujarat high court, in one of the cases, he had to





pay fine for unnecessarily wasting the time of the court.

Dr. Desai is undisputed leader of medical profession in India who takes care of one and all who come to him with any problem which is not against the norms of the law. Once you know him personally, you adore him

2. Clinical trials in India

Interviewer One another topic. In India, as you talked last year, new act on human subject protection was established. Additionally, drug act was revised and guidelines was established to define compensation for research-related injury. There are some news article that because of these situation number of clinical trials is decreasing in India. Also National Institute of Health is going out from India because of this reason²⁶⁾.

Kumar Let me tell you what happened. Global pharmaceutical companies and academic researchers from Europe and United States were coming to India and because of the ignorance, illiteracy and lack of health facilities, they were using people in our country as a guinea pig. They ignored Declaration of Helsinki's guidelines and other rules and regulations. The regulatory bodies like the Indian Medical Council of Medical Research, the Drug Controller general of India and the MCI have the acts to regulate clinical trials. The researchers are trying to bypass the regulations and exploit the poor patients. If I am suffering from tuberculosis and I don't have access to drugs because they're too expensive, and you tell me "Ajay Kumar, come, we will give you free drugs, free everything, and we will give you treatment access in the hospital whenever you want to come." I will be more than happy. I never know why they are doing it. So illiteracy

and ignorance are exploited. Drug trials are being conducted on children, old people and women. The leader of the community in the village is given some pecuniary incentive and then he forces the women, children & old people to take part in the trial. The court of India took notice because there were so much noise from the NGOs and medical professionals. Since the regulations are being strictly followed and public awareness is increasing, drug trials are gradually decreasing.

Interviewer You talked such issue in the last year's presentation in Tokyo. It is very important

for Japanese companies and researchers who are from now going to conduct more clinical trials in developing countries.

Kumar We welcome ethical drug trials in India. I have known Japan and loved the people here for the honesty, integrity and human values. I am sure, Japanese entry into drug trails in India will be most welcomed by us.

Interviewer We appreciate so much such kind words for Japanese researchers.

(Interview: April 25, 2014)



With Dr. Mukesh Haikerwal, second to the right, Chair or the Council, Australian Medical Association

V. Interview with Dr. Miguel R. Jorge, Brazilian Medical Association & WMA DoH Workgroup

1. General situation of medicine and psychiatry in Brazil

Interviewer It is very nice to be able to see you again, as we discussed once when you visited Tokyo last year for the Expert Conference on the Declaration of Helsinki⁹⁾. Now we wish to ask you to introduce the psychiatric medicine in Brazil and the issue of ethics of placebo-controlled clinical trial.

Jorge We are a country of 200 million people where 50 million people has private health insurance and the other 150 million people uses public services. So there is a kind of universal health system provided by the government. But the problem is that the public sector has a lot of problems and does not serve those in need well. Most of the inpatient psychiatric care services the hospitals provide are not good because they receive a fixed amount of money per day, and then for making profits, they spend not much money to provide good services.

For about 20 years now, we saw hospitals closing and the replacement of their care by outpatient services. But the replacement is not going well. First because the number of services offered is quite small considering the needs of the population. Second the services aims to treat mostly those people that were hospitalized before, with severe mental disorders, such as schizophrenia, and bipolar disorder. But there are very few outpatient services aimed for the most prevalent conditions, like depression, anxiety, panic disorders, and phobias. There are some services to treat substance abuse disorders, and very few aiming for children

and adolescent.

On the side of private services, most of the plans offered put stronger limits for psychiatric treatment than for other kinds of health problems. Any form of psychotherapy is almost not allowed or very much restricted.

The other situation is difficult access to services because of stigma. We believe that there are millions of people in Brazil with mental disorders without any kind of treatment and even not been diagnosed with a mental disorder.

2. Long term hospitalization and polypharmacy

Interviewer In Japan formerly many of the schizophrenic patients had been kept in their house and it was called “in house prison”. Now these people are hospitalized and there are not enough community care service. This situation, long term hospitalization is very much criticized not only by Japanese patients groups but also international organization such as World Health Organization.

We have one question. In case the schizophrenic patients are kept inside of the house, is there any governmental inspection system?

Jorge We certainly have, particularly in some regions of our county, a similar situation but not just related to patients with schizophrenia. Many people with mental retardation were found chained at home and there is no governmental inspection for that situation.

Interviewer As a representative of the Brazilian Medical Association, is there any special issues in the field of psychiatry, you are engaged in?

Jorge No, as our partner association, The



Dr. Miguel R. Jorge, Brazilian Medical Association & WMA DoH Workgroup

Dr. Miguel R. Jorge is an Associate Professor of Psychiatry at the Federal University of São Paulo, where he got a Masters of Science (M.Sc.) and a Philosophical Doctor (Ph.D.) degree in Psychopharmacology, and a Full Professorship (*Livre-Docência*) in Clinical Psychiatry.

Prof. Jorge currently is Director of International Affairs of the Brazilian Medical Association and has had some important positions in other health organizations such as President of the Brazilian Association of Psychiatry, Regional Vice-President of the World Federation for Mental Health, and Secretary for Sections of the World Psychiatric Association. He is also a distinguished member of the World Health Organization Panel of Experts on Mental Health.

His main interests are focused on Diagnosis, Classification, Epidemiology, Cultural Issues, Stigma and Clinical Psychiatry, as well as in Medical Education and Ethics. He has published and lectured extensively on these topics in Latin America, Europe, USA, Australia, India and Japan.

Source: http://www.wpanet.org/uploads/About_WPA/Executive_Committee/miguel-jorge-biosketch.pdf

Brazilian Psychiatric Association, is directly responsible for actions related to mental health. The Brazilian Medical Association is more related to push for policies aiming to improve the general rules of healthcare in Brazil.

Interviewer In Japan there is another “rich problem” everybody says, problem of polypharmacy.

Jorge We have a similar problem. In Brazil I think the only 2 classes of medicine for which prescription is duly required are psychotropics and antibiotics. So polypharmacy and abuse of medicine are more related to pain-relief drugs, drugs for allergies, but not psychiatric drugs. However, as the number of psychiatrists in Brazil is not enough, other physicians prescribe a lot of psychiatric medications for their patients. Sometimes drugs are prescribed for patients who do not need such medications. The prescription of antidepressants and benzodiazepines in Brazil has increased a lot in the last decades.

3. Government-owned pharmaceutical manufacturers

Interviewer We know that in Brazil there is some government-owned pharmaceutical manufacturing institute which manufactures some new drug or generic drug and export to developing countries who need access to drug.

Jorge Some generic drugs are produced by few Brazilian government institutes. They produce also HIV drugs and export them to other developing countries where people need them. This is a very particular history, not the rule for every kind of illness. The government also buys drugs from companies to distribute to the people.



4. Medical research and placebo debate

Interviewer So we would like to ask you how is the situation of medical research in Brazil, especially in the area of psychiatry.

Jorge We have 26 states in Brazil, each one with at least one public university. The public universities in Brazil are much better than private universities. There is almost no research outside the public universities in Brazil. Research in psychiatry is consistently done in less than 10 centers in the country.

Most of the research is related to 2 areas, neurosciences and epidemiological research. We have a good journal (*Revista Brasileira de Psiquiatria*) published by the Brazilian Psychiatric Association, with a very good impact factor. Its articles are published in English, not in Portuguese. The journal is freely available in the internet (www.rbppsychiatry.org.br).

We have some governmental agencies that provide grants for research.

We have difficulties for clinical trials in Brazil. The government is very much strict when placebo is to be used. And the process, even when placebo is not included, to get permission for each project, particularly when related to other international centers, takes a long time to be approved. As pharmaceutical companies conduct clinical trials in a multi-national fashion, we lost many opportunities because of this situation.

Interviewer Many of the bioethicist and health activists have concerned ethics of clinical research in developing countries, and have worried about that many of the global pharmaceutical companies have conducted clinical trial in Latin American countries, some of them may be exploitation of trial subjects. If we think about the situation that you explained about psychiatry, we can understand some of them had been exploitation, because there are many treatment-naïve population especially in

the area of psychiatry. It is good chance for company to find good response comparing with placebo group. However, if the government is too much strict, people lose the opportunity. This is very much difficult balance of ethics.

Jorge Ethics frequently requires a balance not always easily reached. So, we have to be careful when recommending a placebo controlled trial and also when conducting research with vulnerable populations such as those from developing countries but we also cannot exclude them from participating in research just because they live in developing countries.

Interviewer “Placebo Conference Sao Paulo 2011” was held by the WMA, 13-15 July 2011, at the Federal University of Sao Paulo. The topics are not only placebo trials (The provision on placebo of 2008 revision of the Declaration), but also “reasonable availability” and “fair benefit” approach, related to “post-trial access” issue.

Jorge As research in general, conferences to discuss them also need to be organized in develop-

ing countries in a way to provide a comprehensive discussion on issues that are of particular interest to research participants from those countries. The Sao Paulo and Cape Town conferences have provided a wonderful environment to advance the discussion on many aspects of the Declaration of Helsinki that are of special interest to developing countries.

(Additional comments, afterwards)

Interviewer In August, Ministries of Health of both countries agreed on memorandum of cooperation in the field of health: first, Pharmaceutical and medical device regulations, in view of improvement in closeness between PMDA (Pharmaceuticals and Medical Devices Agency) and ANVISA (National Sanitary Surveillance Agency); second, sharing knowledge and experience in public health systems; third, policies and strategies for promotion of healthy lifestyles and preventive medicine, including preparations for the ageing society; forth, strengthening health workforce ²⁷⁾.

We hope that this kind of collaboration support



further improvement of health system in Brazil.

Jorge As we say in Brazil, paper accepts everything. We hope that this Memorandum, signed by the Japanese and Brazilian Health Ministries, will not just be a letter of intentions between the two countries but will be effectively implemented

in the near future.

Interviewer We appreciate your kind words, we really hope so.

(Interview: April 26; additional comments, September 2, 2014)



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(Accepted September 30, 2014)

(Published October 30, 2014)