Report

Expert Conference on the Revision of the Declaration of Helsinki in Tokyo
— 2013 revision and perspective toward the 50th anniversary in 2014 *1 —

Chieko Kurihara [1)*2] **Takeo Saio** [2)*3]
1) Editorial Staff, Clinical Evaluation
2) Collaborator to Editorial Committee, Clinical Evaluation

Abstract

In this article, we report on the discussions at the World Medical Association's (WMA) "Expert Conference on the Revision of the Declaration of Helsinki" hosted by the Japan Medical Association (JMA), and held at the Imperial Hotel Tokyo, Tokyo, Japan on February 28 and March 1, 2013. Through the discussions, the proposed draft of the revision of the Declaration came to be clarified. We introduce here some discussion points relating to the proposed draft which was released for public consultation in April 2013, and which will be further discussed and hoped to be finally adopted in October 2013.

The aim of the Conference was to gather opinions and inputs from experts and the expert community, particularly those in Asian countries. We hope that 2013 full-fledged revision of the Declaration is achieved before the commemoration of its 50th anniversary in 2014. The main points discussed during the Conference and during the revision process were the issues of editorial re-construction; compensation for research-related harms; biobank; placebo-controlled trials; resource-poor settings and post-study access; and ethics committees. By collating these discussions, we hope to provide a succinct document for members of the research community in Japan and the world in order to have a better understanding of the 2013 revision of the Declaration and related background discussions.

Key words

Declaration of Helsinki, World Medical Association (WMA), Japan Medical Association (JMA), protection of human subjects, ethical principle of medical research

---

*1 Original version of this article is in Japanese and is included in the Japanese journal *Rinsho Hyoka* (*Clin Eval*). 2013 ; 41 (2) : 337-49. Citation of this English version : Kurihara C, Saio T. Expert Conference on the Revision of the Declaration of Helsinki in Tokyo — 2013 revision and perspective toward the 50th anniversary in 2014 —. *Rinsho Hyoka* (*Clin Eval*). 2013 ; 41 (2) e. (http://homepage3.nifty.com/cont/41_2/p337-49eng.pdf)

*2 Molecular Imaging Center, National Institute of Radiological Sciences

*3 Fuji Toranomon Health Promotion Center, an associate member of the World Medical Association, member of the Japan Medical Association

1. Introduction: Overview of the 2013 revision of the Declaration of Helsinki

"The Declaration of Helsinki: Ethical principles for medical research involving human subjects" by the World Medical Association (WMA) was first adopted in 1964, and 2014 will mark its 50th anniversary. Since its inception, the Declaration has undergone 6 full revisions and 2 partial revisions by adding Notes of Clarification. The WMA convened an "Expert Conference on the Revision of the Declaration of Helsinki" on February 28 and March 1, 2013 at the Imperial Hotel Tokyo, Tokyo, Japan, hosted by the Japan Medical Association (JMA). Following this Conference, the WMA have been preparing full-fledged revision, which we hope to be adopted at the General Assembly in October 2013.

Since the last revision in 2008, the WMA have held several Expert Conferences. Most notably the Conferences in Brazil in 2010 and in 2011 in Sao Paulo were held in order to have intensive discussions on "hot issues" concerning placebo-controlled clinical trials. Additionally, Expert Conferences have been held in Rotterdam, Netherlands and in Cape Town, South Africa both in 2012, also focusing on clinical trials in resource-poor settings and post-study access issues. This time, the aim of the Tokyo Conference was to gather opinions of experts particularly from Asian countries, following the discussions in Brazil and South Africa. We hope a complete revision of the Declaration would be prepared for the 50th anniversary commemoration. The agenda for this Tokyo Conference is shown in Box 1 (page 6, 7).

After the Tokyo Conference, the proposed revision of the Declaration was released for public consultation on April 16, 2013 (with the deadline for submission of opinions set for June 15, 2013). More than 120 opinions were submitted. Considering these opinions, further revised draft was discussed

Reception at the time of opening of the "Expert Conference on the Revision of the Declaration of Helsinki" (Imperial Hotel Tokyo, February 28, 2013)

at the WMA conference in Washington D.C. on August 26, 2013, and we hope that the final version of the revision is adopted at the General Assembly of the WMA to be held in Brazil on October 16-19, 2013.

The following main topics were discussed during the process described above and were included in the proposed revision:

●Issues discussed during the Tokyo Conference and included in the proposed revision:

- Editorial re-construction including adding subheadings to make the document more reader-friendly;
- Strengthen the concept of compensation for research-related harms;
- Add the concept of biobank/biobanking;
- Provide logical clarification on ethical acceptability of placebo-controlled clinical trial (not discussed in the Tokyo Conference but included in the proposed revision);
- Greater consideration for research in resource-poor settings and post-study access;
- Strengthen protection of vulnerable populations;
- Transparency and strengthening the functions of research ethics committee.

●Other important points to consider in the proposed revision:

- Add ideas that will ensure risk minimization and strengthen monitoring by the researcher.
- Strengthen ethical obligation to design and to conduct research subsequently after the therapeutic use of unproven intervention on a patient.

The following are excerpts of the lectures and discussions during the Tokyo Conference on the above-mentioned points. The title and affiliation of each lecturer are shown in Box 1.

2. Discussions at the WMA Expert Conference in Tokyo

2.1 Welcome address

Dr. Yoshitake Yokokura, President of the Japan Medical Association (JMA) and Prof. Fumimaro Takaku, President of the Japanese Association of Medical Sciences opened the Conference by delivering congratulatory addresses and welcoming remarks on behalf of their respective organizations. Their speeches were followed by an address from Dr. Cecil B. Wilson, President of the World Medical Association. The author (Kurihara) had the opportunity to interview Dr. Wilson during the morning coffee break on the first day of the Conference. Below is an excerpt from Dr. Wilson's speech and comments during the interview:

Comments by Cecil B. Wilson, President of the World Medical Association

The World Medical Association is a global federation of 102 national medical associations representing millions of physicians worldwide. The Association endeavors to achieve the highest possible standards of medical care, ethics, education, and health-related rights for all peoples. Those physicians who came together to form the WMA in 1947 understood that an organization was needed to become the authoritative voice on global standards of medical ethics and professional conduct. From the beginning, the WMA has codified these standards in its international code of medical ethics and the Declaration of Geneva (also known as the modern Hippocratic Oath). Other declarations from the WMA which were developed over the years have addressed issues such as patient safety, medical ethics, advanced technology, end-of-life care, access to care, protection of medical personnel in times of armed conflict, and more recently the use of social

Cecil B. Wilson, MD, President, World Medical Association

Cecil B. Wilson, MD, an internist from Winter Park, Florida, USA, was inaugurated as President of the World Medical Association (WMA) in October 2012 at its General Assembly meeting in Bangkok, Thailand. Dr. Wilson is Chair of the American Medical Association (AMA) delegation to the WMA. He has served as a member of the WMA committees on Medical Ethics, Finance and Planning and Socio-Medical Affairs. In addition, he has served for the past three years as a private sector advisor to the United States Delegation to the World Health Assembly at the World Health Organization in Geneva. He served as the 165th president of the AMA from June 2010 to June 2011. He was a member of the AMA Board of Trustees (BOT) and served as chair of the AMA-BOT from 2006 to 2007.

Quoted from the following source：http://www.wma.net/en/60about/40leaders/CV_Cecil_B_Wilson_WMA_President_2012-13.pdf

media. But perhaps there's no clearer example of addressing ethics in medicine than the Declaration of Helsinki.

The Declaration of Helsinki is the loadstone that guides physicians, governments and industry in the arena and dais of doing medical research on human subjects. The purpose of the Conference in Tokyo is to look at potential revisions of the Declaration; not to change core principles but to determine where more guidance is needed to respond to the complexities of a changing world.

There are a number of issues that will be discussed at the Tokyo Conference, such as informed consent, ethics committees and placebo use where there is actually a proven effective treatment. These are already in the Declaration, but whether or not they need to be revised should be considered. Other things, such as biobanking, are actually not in the Declaration yet and should also be considered as we are seeing rapid progress in this area.

The Declaration was first adopted in Helsinki, Finland, and it was presented to the President of Finland. Next year, 2014, the WMA will commemorate the 50th anniversary of the Declaration. The WMA hopes to have the new revised document to present at the 2014 General Assembly.

2.2 Opening remarks, keynote speeches, biobank

Dr. Ramin Parsa-Parsi, Chair of WMA Declaration of Helsinki Workgroup (DoH-WG) delivered the opening remarks, giving a brief background and the report of the activities of the WG. Dr. Parsa-Parsi then introduced Prof. Urban Wiesing, University of Tuebingen, Germany, a member of the DoH-WG, who gave the first keynote speech. Prof. Wiesing explained that as an ethical principle, the Declaration of Helsinki should be, as much as possible, short enough to be read through in a short time. As such, the current revision includes editorial re-construction of the provisions (including adding sub-headings) to make the Declaration a more reader-friendly document. He emphasized

that the Declaration is different from the ICH-GCP which is a technical document.

The second keynote speech was delivered by Prof. Heather Widdows, a philosopher and ethicist from the University of Birmingham (UK). Her speech, which served as a prelude to the discussion on biobanks, included a lecture about the regulation and actual management of biobanks in the United Kingdom. She offered some ideas and considerations concerning issues of genetic research and biobanking, which may be included in the revision of the Declaration.

The first session of the Conference was devoted on the topic of Biobanks, with Prof. Ryuichi Ida from Doshisha University giving the first talk. Prof. Ida proposed necessary ethical considerations in depth about the organization and management of biobanks. This was followed by the presentation of Prof. Alastair Campbell, Centre for Biomedical Ethics, National University of Singapore, who discussed ethical considerations in biobanking. He discussed the management of biobanks in Singapore.

There have been substantial discussions on the issues of broad consent, withdrawal of consent, confidentiality and governance framework. In the proposed revision released for public consultation, the idea of biobanks was included in the paragraph concerning individual-identifiable human material or data. The proposed revision says that where consent would be impossible or impracticable, research may be done only after consideration and approval of a research ethics committee. This is quite similar to the conditions described in the Japanese Ethical Guidelines of Clinical Research (These guidelines are under discussion for revision in 2013).

2.3 Compensation for research-related harms

The first session topic during the second day of the Conference was on "Insurance/Compensation/Protection". Prof. Tatsuo Kuroyanagi, Attorney-at-law, Legal Advisor of the JMA, raised the issue of the discrepancy between the rules on research-related injuries for clinical trials under the Pharmaceutical Affairs Law and the rules for research under the Ethical Guidelines of Clinical Research in Japan. He also introduced some examples of actual amounts of compensation as contained in the insurance agreements by some companies. He pointed out the insufficiency of the current situation of providing compensation in Japan, from the view of human subject protection. On this point, Kurihara commented that after the publication of the article featuring the discussion between

Welcome address

Prof. Fumimaro Takaku
(President of the Japanese Association of Medical Sciences)

Keynote speech

Prof. Urban Wiesing
(University of Tuebingen)

Prof. Heather Widdows
(University of Birminghan)

Session 1: Biobanks

Prof. Ryuichi Ida
(Doshisha University)

Prof. Alastair Campbell
(National University of Singapore)

Box 1

Expert Conference on the Revision of the Declaration of Helsinki

28 February - 1 March 2013, Tokyo
Imperial Hotel Tokyo, Tokyo, Japan

Agenda

Day 1 – Thursday, 28 February 2013 – Sakura Room

2:00 Welcome address
Yoshitake Yokokura, President of the Japan Medical Association (JMA)
Fumimaro Takaku, President of the Japanese Association of Medical Sciences
Cecil B. Wilson, President of the World Medical Association (WMA)

2:15 Welcome remarks
Tetsuya Yajima, Health Service Bureau, on behalf of Norihisa Tamura, Minister, Ministry of Health, Labor and Welfare, Japan

2:20 Opening remarks
Ramin Parsa-Parsi, Chair of the WMA DoH Workgroup, Germany

2:30－3:45 Keynote speeches
Chair: Ramin Parsa-Parsi, Chair of WMA DoH Workgroup

2:30 Keynote speech 1
Urban Wiesing, University of Tuebingen, WMA DoH Workgroup, Germany

3:00 Keynote speech 2
Heather Widdows, University of Birmingham, UK

3:30 Discussion

3:45 Coffee break

4:15－5:30 Session 1: Biobanks
Chair: Masami Ishii, JMA, Vice-Chairman of Council of the WMA & WMA DoH Workgroup
Chair: Miguel R. Jorge, Brazilian Medical Association & WMA DoH Workgroup

4:15 Ryuichi Ida, Doshisha University, Japan

4:35 Alastair Campbell, Centre for Biomedical Ethics, National University of Singapore, Singapore

4:55 Discussion

5:30 End of Day 1

Day 2 – Friday, 1 March 2013 – Hikari Room

9:00－10:15 Session 2: Insurance/compensation/protection
Chair: Wonchat Subhachaturas, Past President of the WMA, Thailand
Chair: Torunn Janbu, Chairperson of WMA Medical Ethics Committee & WMA DoH Workgroup member, Norway

9:00 Tatsuo Kuroyanagi, Legal Advisor of the JMA, Japan, and of the WMA Medical Ethics Committee

9:15 Daniel Fu-Chang Tsai, Department of Social Medicine, National Taiwan University College of Medicine, Taiwan

9:30 Elmar Doppelfeld, Council of Europe, Co-Editor of World Medical Journal, Germany

9:45 Discussion

10:15 Coffee break

10:35－11:50 Session 3: Resource poor settings / Post-study arrangements
Chair: Dong Chun Shin, Chairman of Council of the CMAAO, South Korea
Chair: Poul Jaszczak, Danish Medical Association & WMA DoH Workgroup
10:35 Somkiat Wattanasirichaigoon, Scientific Session of the Medical Association of Thailand & Faculty of Medicine, Srinakarinthwirot University, Thailand
10:50 Prijo Sidipratomo, Indonesian Medical Association Medical Ethics Committee, Indonesia
11:05 Jose Asa Sabili, Philippine Medical Association, Philippines
11:20 Discussion
11:50 Lunch

1:20－2:20 Session 4: Vulnerable groups
Chair: Ming-Been Lee, President of the CMAAO, Taiwan
Chair: Mukesh Haikerwal, Chairman of Council of the WMA, Australia
1:20 Bomoon Choi, College of Medicine, Catholic University of Korea, & Korean Society for Medical Ethics, Republic of Korea
1:35 Ajay Kumar, Indian Medical Association, India
1:50 Discussion

2:20－3:10 Session 5: Ethics Committees
Chair: Margaret Mungherera, Uganda Medical Association & President-Elect, World Medical Association
Chair: Peter Carmel, American Medical Association & WMA DoH Workgroup
2:20 Kaori Muto, Department of Public Policy, Institute of Medical Science, University of Tokyo, Japan
2:40 Discussion
3:10 Coffee break

3:30－4:15 Session 6: General Comments
3:30 James McCormick, U.S. Embassy Tokyo, on behalf of the U.S. Department of Health and Human Services (HHS)
3:35 Yasuyuki Sahara, Research and Development Division, Ministry Health, Labor and Welfare (MHLW), Japan
3:40 Isao Teshirogi, Japan Pharmaceutical Manufacturers Association (JPMA)
3:45 Salvatore Alesci, Scientific Affairs, Pharmaceutical Research and Manufacturers of America (PhRMA)
3:50 Discussion

4:15－5:15 Consensus building / summing up
4:15 Round table discussion
Facilitator: Jeff Blackmer, Canadian Medical Association & WMA DoH Workgroup
Facilitator: Peter Carmel, American Medical Association & WMA DoH Workgroup
4:45 Closing & next steps
Otmar Kloiber, Secretary General of the WMA, Germany
Tai Joon Moon, President Emeritus of the KMA, former President of the WMA, South Korea
Takashi Hanyuda, Vice-president of the JMA
5:15 End of Day 2

Kuroyanagi and another Japanese attorney-at-law, Tadahiro Mitsuishi [1] in the journal *Clinical Evaluation*, the attitude of Japanese pharmaceutical companies has been changing towards the trend of providing a wider range of compensation to injured research subjects. Additionally, the results of a survey by a task force lead by Prof. Hiroshi Watanabe [2] revealed a high rate of Japanese companies granting compensation for injured patients, although this survey has some limitations. This improvement in the situation and trend in compensation for research-related injuries in Japan is one of the achievements of Prof. Kuroyanagi.

Prof. Daniel Fu-Chang Tsai from the National Taiwan University reviewed international norms, laws and regulations concerning research-related injuries, and introduced the situation in Taiwan where it recently, became mandatory, under the law on medical care, to explain about compensation for research-related injuries in the process of obtaining informed consent. Because of this, the number of insurance contracts providing compensation for research related injuries has been increasing. The next speaker, Prof. Elmar Doppelfeld, from the Council of Europe, introduced the issue of compensation in the Additional Protocol to the Convention on Human Rights and Biomedicine concerning biomedical research [3] issued by the Council of Europe. He commented that there is already a provision that covers the issue of compensation for research

◘Session 2: Insurance/compensation/protection

From the left, Prof. Daniel Fu-Chang Tsai (National Taiwan University), Prof. Tatsuo Kuroyanagi (Legal Adviser of Japan Medical Association), Prof. Elmar Doppelfeld (Council of Europe)

related harm in this European document and instruments of the Council are the only international protective legal instruments covering all medical research on human beings, and that the actual realization of such a provision will depend on the establishment of relevant laws and regulations by governments in each country.

2.4 Resource poor settings, post-study arrangements, and vulnerable populations

Since the 1990s, issues and ethical challenges relating to clinical research in resource-poor settings and post-study access to the therapy proven to be beneficial have been the subject of debates. The major contention in these debates is that rich countries conduct clinical research in a resource-poor region, but the therapy or drugs proven to be effective during the research becomes available only in rich countries and not in the poor regions. So the countries sponsoring such research are accused of exploiting the vulnerability of research subjects in those poor countries. The WMA responded to this debate, and through these intensive debates, adopted a 2000 revision subsequently adding a Note of Clarifications in 2004 to the 2000 version of the Declaration. Additionally, in the 2008 revision, the WMA made an even more emphatic position and now has reached the 2013 proposed revision.

Session 3: Resource poor settings/Post-study arrangements

From the left, Dr. Prijo Sidipratomo (Indonesian Medical Association), Dr. Somkiat Wttanasirichaigoon (Medical Association of Thailand), Dr. Jose Asa Sabili (Medical Association, Philippines)

Prof. Somkiat Wattanasirichaigoon, Medical Association of Thailand, Dr. Prijo Sidipratomo, Indonesian Medical Association, and the Dr. Jose Asa Sabili, Philippine Medical Association each reported on the situation in their respective countries and the efforts being made to develop medical research governance framework in conducting research in resource-poor settings to ensure the protection of patients participating in such research. Dr. Sabili particularly raised a new issue about the disposal of research drugs and materials and the impact of such disposal on the environment. In the session on "vulnerable groups", Dr. Ajay Kumar of the Indian Medical Association raised the issue of exploitation of research subjects in his country where naive patients, who cannot access medicines or treatments due to economic reasons, have participated in clinical trials sponsored by multinational companies; yet the majority of these patients cannot access even basic medical treatment. He stressed that "honesty" of sponsors and researchers is significantly important in order to avoid exploitation.

Prof. Bomoon Choi, Catholic University of Korea and Korean Society for Medical Ethics, talked about categorizing vulnerable groups in the Declaration and expressed an opinion that it is not appropriate to put too much detailed description of this categorization in the Declaration.

In response to these discussions, the proposed

Session 4: Vulnerable groups

From the left, Prof. Bomoon Choi (Catholic University of Korea), Dr. Ajay Kumar (Indian Medical Association)

revision now includes the following statement: "*All vulnerable groups need specifically considered protection; medical research involving a disadvantaged or vulnerable population or community is only justified if the research is responsive to the health needs and priorities of this population or community and the research cannot be carried out in a non-vulnerable population; this population or community should stand to benefit from the knowledge, practices or interventions that result from the research.*"

During the Q&A forum, Kurihara asked the lecturers for their opinion regarding the changing trend among the bioethicists in the U.S., especially in the U.S. National Institutes of Health, who believe that vulnerable populations should not be excluded from the opportunity to participate in research without justifiable reason to exclude them [4]. The idea is that if research involving vulnerable population is limited to those studies which cannot be carried out in a non-vulnerable population, patients in the vulnerable population will not be able to get early access to new therapeutic treatments which could possibly benefit them also but which were studied only using non-vulnerable population groups. Some of the lecturers responded that such an idea is a little bit "tricky". In another situation, Kurihara asked for the opinions of the lecturers on the idea that the CIOMS guidelines [5] provides that the conduct of a research which could contribute to capacity development of community is justified even if the sponsors of such research cannot provide post-study access. Some of the lecturers said that capacity development is the obligation of the national authority.

Our general impression was that the lecturers representing developing countries expressed a strong wish to avoid exploitation of research subjects in their regions rather than in seeking benefits by means of participating in global companies' multinational clinical trials.

2.5 Ethics Committees

In the session on Ethics Committees, Prof. Kaori Muto, Institute of Medical Science, University of Tokyo, reported on her analysis of ethics committees from viewpoint of a sociologist, by reviewing the academic literature. Her analysis revealed that a recent trend in academic discussions is to focus not only on traditional functions of an ethics committee, but more on issues relating to quality assurance, efficient management of an ethics committee, and the joint review of multicenter clinical studies. Participants discussed focusing on the necessity of dual review especially in the case of collaborative studies between rich and resource-poor countries and on another point concerning the review of non-medical (social, psychological, etc.) research.

In the proposed revision of the Declaration, new wordings were added to emphasize the necessity of ensuring transparency of the committee and the qualifications of such a committee (committee "must be duly qualified").

2.6 General comments

In the session on General Comments, Dr. James McCormick of the U.S. Embassy Tokyo, read a statement on behalf of the U.S. Department of Health and Human Services. Other delegates in this group session – Dr. Yasuyuki Sahara, Ministry of Health, Labour and Welfare (MHLW) in Japan, Dr. Isao Teshirogi, Japan Pharmaceutical Manufacturers Association (JPMA) introduced the Japanese regulatory framework and their activities; and Dr. Salvatore Alesci, Pharmaceutical Research and Manufacturers of America (PhRMA) – briefly stated their comments. Historically, the U.S. government and the American Medical Association have submitted several comments to the WMA when there are principles in the Declaration which did not fit U.S. regulations or the actual situation in the conduct of clinical trials. Companies engaged in

global clinical trials often avoid quoting the newest version of the Declaration in their protocols. Therefore, the comments of the U.S. representatives have attracted our attention. They have expressed explicit opinions on the issues of compensation, post-study access, etc., and their general opinion is that the Declaration should describe fundamental principles and that actual detailed rules should be described in national laws and regulations of each country.

2.7　Consensus building, summing up, and closing

In the session on "Consensus building / summing up", Dr. Jeff Blackmer of the Canadian Medical Association and Dr. Peter Carmel of the American Medical Association (both members of WMA DoH-WG) summed up the discussion and explained the direction of the revision process. The next revision stage will strengthen the principles of the Declaration to provide compensation for research-related harms; to protect research subjects in resource-poor settings and of vulnerable groups; to assure transparency in clinical research, and to improve the function of ethics committees.

In closing, Dr. Otmar Kloiber, Secretary General of the WMA, Prof. Tai Joon Moon, President Emeritus of the KMA (Korean Medical Association) and former President of the WMA, and Dr. Takashi Hanyuda, Vice President of the JMA, gave speeches.

2.8　Other issues discussed

The relationship between the Declaration and national laws and regulations was discussed several times during the Conference. Various opinions have been expressed about the differences between ethical principles and legal regulations, i.e. whether legally-binding regulations work sufficiently to promote ethical conduct in research or whether the soft-law framework with ethical principles and guidelines is enough.

There are other important points which were not

Session 5: Ethics Committees

Prof. Kaori Muto
(University of Tokyo)

Consensus building/summing up

The scenery of the conference at the time of "closing & next steps"

discussed during the Tokyo Conference. One is the issue of placebo-controlled clinical trials which was discussed at the Expert Conferences in Brazil in 2010 and 2011. We were privileged to have discussed this issue during an interview with Dr. Otmar Kloiber. An article [6] on this interview also appears in this current issue of the journal *Clinical Evaluation*. This journal has published in the past several articles related to the revisions of the Declaration [7~11], and international journals have published a substantial number of academic literature on this point.

Additionally, the following 2 points included in the proposed revision are especially important:

- To add ideas to ensure risk minimization and monitoring by the researcher.
- To strengthen ethical obligations to design and conduct research subsequently after the therapeutic use of an unproven intervention on a patient.

The importance of risk minimization necessitates adding a principle to address it. Over the last decade, we have seen some rapid development and advancement in medical knowledge leading to the integration of various interdisciplinary knowledge. The integration of various fields of medical knowledge is important in developing "risk-minimization" strategies. It is also important to consider the importance of "monitoring", especially in Japan where recently, scientific misconduct has been exposed and discussed more often. We are now seriously discussing the issue of "monitoring and audit" which is required under the GCP Ordinance but not under the Ethical Guidelines for Clinical Research.

Another important issue to consider in the revision is the conduct of research involving unproven intervention. In the previous version of the Declaration, such research was allowed for the purpose of saving the life of a patient, subject to strictly defined conditions, with the recommendation that "such an intervention should be made the object of research, where possible." In the proposed revision, the words "where possible" have been deleted, and the ethical obligation of physicians is strengthened by requiring them to make such an intervention the object of research subsequently after the administration of such unproven treatment to a patient in defined conditions. In Japan, the logical boundary between research and practice has not been explicitly defined and understood, so we should learn from this strengthened principle.

2.9 Press Conference

The authors participated in the press conference held after the closing of the Conference. Dr. Yoshitake Yokokura, President of the JMA, Dr. Masami Ishii and Dr. Hiromi Ishikawa, both executive directors of JMA, Dr. Otmar Kloiber WMA Secretary General, Dr. Ramin Parsa-Parsi, Chair of the WMA DoH-WG fielded questions from the journalists. The perspectives of WMA and JMA expressed during the press conference have clarified the view that Asian experts are seeking stronger protection of human research subjects. We expressed our gratitude that this kind of opportunity for open discussion was provided, and WMA expressed their appreciation for the excellent organization and hospitality of the JMA.

3. Conclusion

The primary reason for holding this Expert Conference was to hear the opinions of Asian experts. In recent years we have visited Asian hospitals and have been holding discussions with medical professionals. From these experiences and discussions with Asian experts during the Conference of this time, we were surprised at the rapid progress in and superiority of Asian medical systems far better than Japan. On the other hand, the systems have not

Press Conference

Dr. Yoshitake Yokokura
President,
Japan Medical Association

Dr. Masami Ishii
Executive Board Member,
Japan Medical Association

Dr. Hiromi Ishikawa
Executive Board Member,
Japan Medical Association

Dr. Otmar Kloiber
Secretary General,
World Medical Association

Dr. Ramin Parsa-Parsi
Chair of DoH-WG, WMA
German Medical Association

Press Conference after the closing of the Conference

developed enough to be shared by all the citizenries in some of those countries. This Expert Conference provides an important opportunity to consider such Asian situations as well as the ethical principles expressed in the Declaration. It is interesting to note that most of the lecturers in this Conference have expressed strong opinions seeking for protection of human research subjects from the perspectives of the people who have difficulty accessing the benefits resulting from the development of medical technologies.

The Conference has attracted a distinguished roster of attendees, not only eminent lecturers from various health fields, but also medical experts including representatives of medical associations from each member state and experts in medical ethics, providing a vivid and lively discussion of the topics and issues raised. Japanese participants also expressed their opinions and questions concerning ethical conduct in international clinical research and sometimes from the perspective of developing countries. Needless to say, the Conference was a precious opportunity for international exchange among medical and ethics professionals.

In recent years in Japan, the long targeted goal to participate in a global clinical development program has been mostly achieved, and academia-initiated international clinical development has been promoted. While it is uncertain which of the principles described in the proposed revision will be adopted in October, it is certain that all the proposed ideas discussed during the revision process are worthy to keep in our minds and hearts. This time, we should sincerely consider the voices of our colleagues from Asia which were expressed during the Conference and in the proposed revision. We hope that all members of the Japanese and the world research communities will deeply understand the forthcoming 2013 revision of the Declaration of Helsinki and the background discussions culminating to this revision.

Acknowledgement

We greatly appreciate the World Medical Association and the Japan Medical Association to provide this precious opportunity to participate in the Conference and also to give great support for development and publication of this article.

REFERENCES

1) Kuroyanagi T, Mitsuishi T. Discussion on Paragraph 30 of the Declaration of Helsinki and the issue of compensation in the NDA (new drug application) trials in Japan. *Rinsho Hyoka (Clin Eval)*. 2003 ; 31 (1) : 129-39. Japanese.
2) Watanabe H, et al. Protection of human subjects and compensation for research-related injuries Proposal of explanation sheet based on survey of the actual status in Japan. *Rinsho Hyoka (Clin Eval)*. 2011 ; 39 (1) : 5-29. Japanese.
3) Council of Europe. Additional protocol to the convention on human rights and biomedicine concerning biomedical research. Strasbourg Jan 25, 2005. (European Treaty Series No. 195.)
4) Kurihara C. Ethics in research involving children: introduction — Historical review over ethical dilemma and regulatory development in the world —. *Rinsho Hyoka (Clin Eval)*. 2007 ; 34 (1) : 103-22. Japanese.
5) Council for International Organizations of Medical Sciences (CIOMS). International Ethical Guidelines for Biomedical Research Involving Human Subjects. 2002.
6) Kloiber O. Interviewed and translated by Kurihara C, Saio T. Discussion toward the 50th anniversary of the Declaration of Helsinki — Interview with Dr. Otmar Kloiber, Secretary General, World Medical Association —. *Rinsho Hyoka (Clin Eval)*. 2013 ; 41 (2) : 351-72. Japanese.
7) Levine RJ, Tsutani K, Sakanoue M, Mitsuishi T, Kawai S, Sato K, Kakee N. Round table discussion: Ethics in clinical trial in the days of globalization of drug development. *Rinsho Hyoka (Clin Eval)*. 1999 ;

26(3)：341-80. Japanese.
8) Sakanoue M. Recent movement at the World Medical Association on revision of the Helsinki Declaration. *Rinsho Hyoka (Clin Eval)*. 1999；26(3)：395-408. Japanese.
9) Levine RJ, Lurie P, Lagakos SW, Interviewed by Kurihara C. Interview with Robert J. Levine, Peter Lurie and Stephan W Lagakos: Discussion on the Declaration of Helsinki and its background. *Rinsho Hyoka (Clin Eval)*. 2001；28(3)：409-22. Japanese. Available form：http://homepage3.nifty.com/cont/28-3/contents_e.html
10) Human D. Interviewed by Kurihara C, Mitsuishi T. Interview with Delon Human, Secretary General of the World Medical Association: Discussion on the 2000 revision to the Declaration of Helsinki and onwards. *Rinsho Hyoka (Clin Eval)*. 2002；29(2･3)：307-13. Japanese.
11) Tsuboi E. Interviewed by Kurihara C. The 2000 revision of the Declaration of Helsinki and its implications in medical ethics: Interview with the WMA Immediate Past President, Eitaka Tsuboi. *Rinsho Hyoka (Clin Eval)*. 2002；30(1)：99-107. Japanese.

＊　　＊　　＊