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REPORT

**MEETING ON THE REVISION OF GUIDELINES
FOR CLINICAL RESEARCH ON ACUPUNCTURE**

Convened by:

**WORLD HEALTH ORGANIZATION
REGIONAL OFFICE FOR THE WESTERN PACIFIC
Seoul, Republic of Korea
24 – 26 August 2005**

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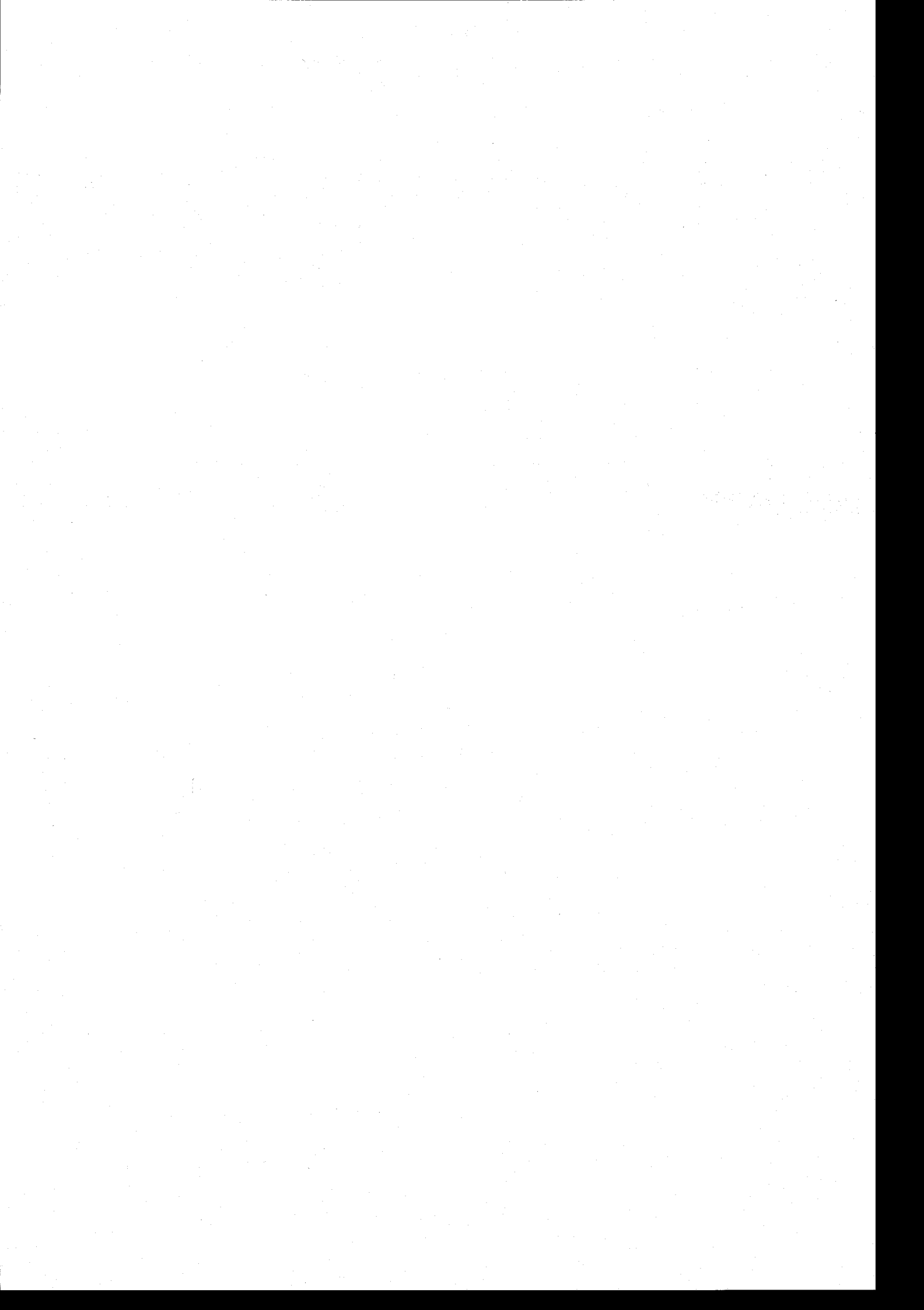
NOTE

The views expressed in this report are those of the participants in the Meeting on the Revision of Guidelines for Clinical Research on Acupuncture and do not necessarily reflect the policy of the World Health Organization.

This report has been prepared by the Regional Office for the Western Pacific of the World Health Organization for governments of Member States in the Region and for the participants in the Meeting on the Revision of Guidelines for Clinical Research on Acupuncture held in Seoul, Republic of Korea from 24 to 26 August 2005.

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SUMMARY

The Working Group on the revision of Guidelines for Clinical Research on Acupuncture met in Seoul, Republic of Korea, from 24 to 26 August 2005. The main objectives of the meeting were to review the regional publication, *Guidelines for Clinical Research on Acupuncture* (1995), to make necessary revisions to the *Guidelines*, to make recommendations on further collaboration and activities in the field of research on acupuncture, and to discuss scientific evidence-based approaches in clinical research on acupuncture.

Fourteen members from eight Member States, one secretariat staff member from the WHO Regional Office for the Western Pacific and ten observers from the Republic of Korea attended the meeting.

Professor Sung-Keel Kang was elected Chairperson, Professor Brenda Golianu, Vice-Chairperson and Drs Se-Hyun Kim and Peter White, Rapporteurs. On behalf of Dr Shigeru Omi, WHO Regional Director for the Western Pacific, Dr Seung-Hoon Choi, Regional Adviser in Traditional Medicine, delivered a speech during the opening ceremony.

The Working Group members presented their papers, reviewing the current status of clinical research on acupuncture. The drafts of proposed revisions to the previous *Guidelines* were discussed extensively. The issues covered during the discussions included: the definition of the new terms; reorganization of the section on clinical research design; revision and update of the new nomenclature (e.g., control group); introduction of the Institutional Review Board (IRB) in the section on ethical approval; and inclusion of additional health outcomes, including health-related quality of life (HRQoL), qualitative measures, etc.

In the course of the discussions, the Working Group developed the revised *Guidelines for Clinical Research on Acupuncture*, and made recommendations for promoting their dissemination. A summary of these recommendations follows:

- (1) The use of standard WHO acupuncture nomenclature should be encouraged.
- (2) New nomenclature should be adopted with regard to controls and should be used in the study protocols, thereby assisting in standardization of reporting.
- (3) WHO should encourage journal editors to adopt WHO nomenclature.
- (4) The *Guidelines* should be disseminated in hard copy and also made available electronically to allow worldwide access.
- (5) WHO should encourage Member States to translate the *Guidelines* into their native languages.
- (6) WHO should assist in the dissemination of research findings and their integration into clinical practice (in line with evidence-based medicine).
- (7) WHO should encourage journal editors to publish protocols and preliminary studies. In addition, they should provide space for complex trials to adequately report their methodology.
- (8) WHO should encourage courses and training programmes in acupuncture research methodology to ensure the quality of future trials.

- (9) WHO should encourage education for health professionals in acupuncture terminology, practice and research.
- (10) WHO should encourage further dialog around the *Guidelines* within the home institutions of the participants and other interested parties in order to encourage their application and adaptation.
- (11) WHO should encourage Member States to translate and publish important clinical findings into other Member States' languages.
- (12) WHO should establish international networks and collaborative studies among clinical researchers in acupuncture, thus encouraging the development of high quality clinical trials. In this way, evidence-based practice will be facilitated and health care improved.

1. INTRODUCTION

During the last few decades, acupuncture has spread worldwide. There has been a considerable increase in interest in the therapeutic applications of acupuncture and a desire to explain its modes of action in terms of modern scientific knowledge. In 1995, the WHO Regional Office for the Western Pacific published the *Guidelines for Clinical Research on Acupuncture*, which was a product of the Working Group Meeting on Clinical Research Methodology for Acupuncture held in Aomori, Japan, in June 1994.

Since publication of the *Guidelines* in 1995, there have been significant developments in clinical research on acupuncture. The Regional Office conducted meetings in 1999 and 2003 entitled "Consultation on Traditional and Modern Medicine: Harmonizing the Two Approaches". These meetings strengthened the consensus for evidence-based research in traditional medicine. It was felt that a new Working Group meeting would provide a venue to discuss developments and recommend any revisions to the *Guidelines*.

The Working Group met in Seoul, Republic of Korea, from 24 to 26 August 2005.

1.1 Objectives

The objectives of the meeting were:

- (1) to review the *Guidelines for Clinical Research on Acupuncture*;
- (2) to make necessary revisions to the *Guidelines*;
- (3) to make recommendations on further collaboration and activities in the field of research on acupuncture; and
- (4) to discuss scientific evidence-based approaches in clinical research on acupuncture.

1.2 Participants

The Working Group comprised 14 temporary advisers and one secretariat staff member from the WHO Regional Office for the Western Pacific. Ten observers from the Republic of Korea also attended the meeting. The list of participants is shown in Annex 4.

1.3 Organization

Professor Sung-Keel Kang was elected Chairperson, Professor Brenda Golianu, Vice-Chairperson and Drs Se-Hyun Kim and Peter White, Rapporteurs.

1.4 Opening ceremony

Dr Seung-Hoon Choi, Regional Adviser in Traditional Medicine, WHO Regional Office Western Pacific, spoke on behalf of Dr Shigeru Omi, WHO Regional Director for the Western Pacific, who was unable to attend the opening ceremony. During his speech, Dr Omi pointed out that more than a few clinical studies on acupuncture had been undertaken and included in the Cochrane Database of Systemic Reviews during the last decade, and at the same time there had been growing demands for updated guidelines for clinical research on acupuncture.

During the opening ceremony, Professor Byoung-Soo Cho, Director of East-West Medical Research Institute, Kyung Hee University delivered welcoming remarks. Mr Keun-Tae Kim, Minister of the Ministry of Health and Welfare (substituted by Mr Young-Hak Yoo, Director General of

Oriental Medicine Bureau), Republic of Korea, Dr Jong-Hee Um, President of the Association of Korean Oriental Medicine, and Professor Bong-Arm Rhee, Vice President for Medical Affairs, Kyung Hee University also gave welcome addresses.

2. PROCEEDINGS

2.1 Presentations

The current status of clinical research on acupuncture and the methodology used for clinical evaluation of acupuncture were outlined in the working papers prepared by the Working Groupmembers. The papers submitted are summarized below.

Professor Brenda Golianu, Stanford University, United States of America, reviewed the progress made in paediatric acupuncture research in the last 10 years and the need for further work in that area. She recommended that research and development focused specifically on populations with special needs should be encouraged, including children, the elderly, and populations with physical and mental disabilities. Special considerations may be necessary for such populations. The concurrent conventional medical treatment being received by the subjects should be described and standardized wherever possible. Acupuncture may be combined with non-invasive measures such as acupressure, moxibustion, laser acupuncture or electrical stimulation of points. However, such interventions should be accurately described and controlled in the study design. Researchers should make explicit the type of acupuncture used in studies and assign both Western and Oriental medical diagnosis wherever possible. The CONSORT Statement and STRICTA (Standards for Reporting Interventions in Controlled Trials of Acupuncture) guidelines should be adopted in the reporting of clinical trials.

Professor Kenji Kawakita, Department of Physiology, Meiji University of Oriental Medicine, and Director, Research Department of the Japan Society of Acupuncture and Moxibustion (JSAM), Japan, noted that individualized diagnosis and treatment are essential characteristics of acupuncture therapy. However, randomized controlled trials (RCTs) seem to be an inadequate research design for evaluating efficacy. On the other hand, the n-of-1 trial (single-subject experimental design) has been noted as a useful clinical research design. The n-of-1 RCT was placed at the top of the strength-of-evidence hierarchy in a recent textbook on evidence-based medicine. For each patient, the best therapy is determined by the n-of-1 RCT, where internal validity is very high but external validity is still poor. Multiple, randomized n-of-1 trials are proposed to strengthen external validity. To obtain external validity, patients should be registered and allocated randomly to groups receiving various interventions, including individualized acupuncture, formulated standardized acupuncture and conventional therapies. Each subject receives an intervention (including individualized ones) according to the n-of-1 RCT protocol and the results are evaluated by randomization test. The incidences of positive and negative results in the groups are analysed statistically (chi-square test) and the external validity of individualized interventions can then be evaluated.

Professor Kawakita also noted the importance of moxibustion therapy. The ancient medical literature found in the Mawangdui tombs clearly showed that the concept of Meridians was based on clinical experience of moxibustion rather than acupuncture. From the physiological point of view, the polymodal receptor, one kind of nociceptor, is the key candidate, as it is responsive to both acupuncture and moxibustion.

Professor Se-Hyun Kim, Department of Health Sciences, College of Medicine, Pochon CHA University, Republic of Korea, introduced the concept of health-related quality of life as an outcome measure of clinical research on acupuncture. The term 'health-related quality of life' (HRQoL) refers to the extent to which a person's physical, emotional and social well-being is affected by a clinical condition or its intervention. In clinical trials, the commonly used endpoints are physiological or laboratory measures of response. Although such traditional biomedical measures are often the primary endpoints in clinical trials, they do not reflect how the patient feels and functions in daily activities. In parallel with traditional clinical endpoints, treatment effects may be equivalent physiologically but may differ in impact on functioning and well-being and represent a trade-off between improvements in clinical parameters (e.g., reduction in tumor size, etc.) *versus* a deterioration in functioning and well-being (e.g., nausea and vomiting, etc.). In certain diseases or conditions, the patient's perception of his or her well-being may be the most important outcome (patient-reported outcomes or PROs). In individuals with a chronic condition, where a cure is not attainable, HRQoL may be the essential outcome. Currently, the majority of cancer patients do not receive adequate palliative care. Acupuncture has been shown to be effective in the treatment of pain and nausea among cancer patients, and has also been shown to improve general well-being. Acupuncture has also shown some effectiveness in relieving symptoms of anxiety and depression. Acupuncture trials will evaluate the efficacy of acupuncture in addressing the quality of life and symptoms of patients with chronic diseases and incurable cancers.

Professor Tat-Leang Lee, Department of Anesthesia, National University Hospital, Singapore, reviewed functional brain imaging, as used in research on acupuncture. Functional neuroimaging techniques represent an innovative technological advance in recent neuroscientific research. The non-invasive nature of single photon emission computed tomography (SPECT), positron emission tomography (PET), and functional magnetic resonance imaging (fMRI) have made it possible to visualize, not only the structure, but also the functions of the brain. Researchers have begun to apply these methods to acupuncture research to explore neural correlates of acupuncture efficacy as well as acupuncture's biological mechanisms. A total of 31 reports have been published in this field since the mid-1990s. All the above-mentioned techniques have been used by different investigators. The information obtained so far seems to support the notion of acupuncture point-brain correlation (e.g. vision-implicated acupuncture points and activation of the visual cortex) and modulation of disease-related neuromatrices during acupuncture (e.g. classic analgesic acupuncture points activating and deactivating the hypothalamus and limbic system, respectively). However, the lack of studies on clinical patients makes extrapolation to the clinical situation difficult. Furthermore, there are some design issues particularly pertinent to acupuncture in imaging research.

Professor Liu Baoyan, Vice President, China Academy of Traditional Chinese Medicine, China, presented an assessment of Chinese acupuncture RCT based on studies by the Cochrane Collaboration reported in the Chinese Acupuncture Journal from 1991 to 2004. Altogether, 3775 clinical research articles were published. Professor Liu analysed the quality flaws of 608 RCTs, which revealed significant problems: random concealment was absent in most articles; there were few blind trials; the 'gold standard' was rarely used; and few trials did subject number estimates, confounding the result when an intervention with no confirmed effect was used as a control. Eight systematic reviews of acupuncture were registered in the Cochrane Collaboration. Through those reviews, it was found that high quality clinical trial reports were rare, making the conclusions less reliable. Acupuncture is a typical complex intervention, and therefore it is very important to understand the 'active ingredient' before carrying out acupuncture RCTs. Professor Liu proposed amendments to the *Guidelines*.

Professor Liu Zhishun, Director, Acupuncture and Moxibustion, Guanganmen Hospital, China, addressed quality control in acupuncture clinical research. Acupuncture is a complex intervention whose curative effects depend on many factors. Non-standardization of these factors will affect the total curative effect and research quality, and will compromise the repeatability and creditability of the trial. A quality control system should consist of control of the study design as well as the process. Control of the study design system should involve standardization of point location, depth of insertion, needling angle and direction, needling reaction, style and intensity of stimulation. Quality control of the process should include standardization of acupuncture manipulation and uniformity of training of investigators. The training could be facilitated by making acupuncture manipulation videos and handbooks readily available for bedside reference.

Professor Nguyen Tai Thu, President, Vietnamese Acupuncture Association, Viet Nam, presented a video showing two directions in acupuncture research in Viet Nam.

Professor Ikuro Wakayama, Kansai College of Oriental Medicine, Japan; Editor-in-Chief, *Journal of the Japan Society of Acupuncture and Moxibustion (JSAM)*, summarized the present status of acupuncture clinical research in Japan. Although the number of clinical research studies conducted as RCTs, CCTs (controlled clinical trials) and meta-analysis in Japan has rapidly increased over the past six years, only 26 RCTs research papers have been published over the same period, and the average number of published papers per year in the field of acupuncture and moxibustion is only 4.3, suggesting that the use of RCTs in this field has not yet become well established. However, in the *Journal of the Japan Society of Acupuncture and Moxibustion* there are some signs of change in the approach to clinical research. Among 64 papers recently submitted to the journal, 26 were clinical trials, including RCTs and CCTs, with a few crossover research studies and one n-of-1 trial. Professor Wakayama recommended the following five revisions to the *Guidelines* from the perspective of a journal editor: (1) Reorganize the section on headings for items and sub-items to make it clearer; (2) Prioritize the "Ethical considerations" section; (3) Reorganize the "Classification of the clinical research design" section; (4) Make a checklist of the standard protocol to help researchers; and (5) Publish the *Guidelines* as part of the instructions for journal authors.

Dr Peter White, University of Southampton, United Kingdom, discussed several issues relevant to acupuncture research and suggested changes and/or clarification in several areas. (1) Regarding clarification of terms: only those therapies that use penetrating needles should be called acupuncture. Other 'related' therapies need different labels; there should be clarification of the difference between efficacy and effect and encouragement of transparency in reporting such trials. (2) Regarding controls: guidelines should be set for the appropriateness of different types of control used in a trial so that researchers can be clear as to when to use which control. (3) Regarding treatment: to ensure that treatment regimes are adequate and as pragmatic as possible, a 'Delphi' process should be employed. This should function with some flexibility to allow some individualization of treatment. (4) Regarding outcomes: as well as measuring the primary outcome, efficacy trials should include a range of secondary measures i.e. a nested qualitative perspective, a quality of life measure, a disease-specific measure, safety, economic factors (e.g. quality's). (5) The following general points should be considered: homogeneity of condition (perhaps use of a 'dual diagnosis process i.e. Western and Traditional Medicine); patients should always be blinded; use blind, or at least patient-completed measures; always use a power calculation (except in pilot studies); crossover studies should not be used in efficacy studies for acupuncture; all trials should utilize CONSORT and STRICTA guidelines. WHO should encourage editors to allow for adequate reporting of complex trials such as acupuncture. (6) In conclusion: trials must have internal rigour and clarity. The methodology and the controls used must match up to the question being asked. A trial must not be viewed in isolation, but as part of a coherent programme of research for any particular condition, because different groups (e.g. patients,

G.P.'s, scientists, providers, etc.) are often interested in different aspects of health and no single trial can provide all the answers. Instead, true validation and acceptance of a treatment should include a wide approach and a wide research strategy. All such evidence must be reviewed before drawing conclusions.

Professor Hitoshi Yamashita, Tsukuba College of Technology Clinic, Japan, summarized the following: (1) Pragmatic trials: Many acupuncture RCTs focus on detecting the 'specific effect' of acupuncture by setting sham, superficial or minimal needling as a control. However, setting an inert placebo acupuncture group is almost impossible because even very slight stimulation on the skin can cause physiological responses. There should be more description of pragmatic trials in the revised *Guidelines*. A pragmatic trial may include a current standard treatment as a control group, individualized treatment, individualized outcome measures, etc. (2) Adverse events: Reporting adverse events should be explained in more detail, together with definitions (unfavourable medical events during or after treatment regardless of causal relationships), in an independent section with a heading in the revised *Guidelines*. Safety information is important, not only because it allows assessment of the risk-benefit balance, but also because the negative aspects as well as the positive aspects of acupuncture must be disclosed. (3) Research ethics: The revised *Guidelines* should encourage authors to declare a conflict of interest and to register their clinical trial protocol in order to avoid publication bias and injustice. (4) Standardization of the quality of reports: Once an RCT paper is published, it will be included in systematic review or meta-analysis. The authors of acupuncture RCT should follow the CONSORT Statement and STRICTA recommendations.

Professor Chris Zaslowski, Department of Health Sciences, College of Traditional Chinese Medicine, University of Technology, Australia, stated that there had been increasing interest in the use of human research ethics to guide the design and conduct of acupuncture clinical trials. In addition to ensuring protection of the welfare and rights of the research participants, consideration of ethics facilitates research that will be of benefit to humankind. Ethical research considers the values of the research's merit and integrity, including respect for human beings and weighing up of the risk-benefit and justice. The acupuncture trial design should use recognized principles of research conduct. Acupuncture research design should mimic, as closely as possible, clinical practice. Possible design options are 'double screening' of participants using both Western medical criteria as well as pattern identification (*bian zheng*). Ethical consideration also needs to be given to partial consent and participant deception when using a sham control. Partial consent may be justified if the target illness does not demand urgent attention, the risk can be adequately assessed and managed and the participants are explicitly informed that they will not receive any information on the specific goals of the interventions. Finally, ethical consideration should be given to the use of placebo controls. Placebo controls may be justified if there are scientifically compelling reasons to determine the safety and efficacy of acupuncture and when no additional risk is associated with delaying an effective treatment.

2.2 Discussion

Professor Sung-Keel Kang, Department of Acupuncture and Moxibustion, College of Oriental Medicine, Kyung Hee University, Republic of Korea, presented proposed revisions to the previous version of the *Guidelines for Clinical Research on Acupuncture*, published in 1995. The proposed revisions were prepared by the Korean experts group, consisting of Professor Sung-Keel Kang, Department of Acupuncture and Moxibustion; Professor. Hi-Joon Park, Department of Meridian and Acupuncture, College of Oriental Medicine, Kyung Hee University; Professor Se-Hyun Kim, Department of Health Sciences, College of Medicine, Pochon CHA University; and Professor. Jung-Chul Seo, Department of Acupuncture and Moxibustion, Daegu Haany University, Republic of Korea

(all temporary advisers for the meeting); as well as Professor Yong-Suk Kim and Professor Do-Young Choi, Department of Acupuncture and Moxibustion; Professor Sabina Lim, Department of Meridian and Acupuncture; Professor Kyung-Eh Ahn, East-West Medical Research Institute, Kyung Hee University; and Professor Sang-Woo Kim, Bundang CHA Oriental Medical Hospital, Republic of Korea (all observers at the meeting). Over a 10-month period, the temporary advisers worked with the observers on changes and additions in structure, terms, contents, etc for their revised draft of the *Guidelines*.

The proposals put forward by the Korean experts group for discussion included: introducing the Institutional Review Board (IRB) in the section on general considerations as an ethical issue; uniting the Glossary, formerly divided into two major categories, to arrange the terms and newly added terms in alphabetic order; reorganizing the section on clinical research design; revising and updating the contents (i.e. blinding, randomization, control group, crossover, etc); and introducing new research designs (i.e. factorial design, cross-sectional studies, case series, etc) and outcomes, including health-related quality of life (HRQoL). In addition, Professor Sung-Keel Kang suggested that acupuncture clinical research differs in character from other forms of clinical trial, since the practice of acupuncture has many unique features. The nature of acupuncture treatment therefore should be thoroughly considered when deciding on a research hypothesis, study design, therapeutic methods and outcome measures, etc. New research strategies, such as pragmatic trials, individualized acupuncture treatments or cost-effectiveness studies, are also warranted to assess contemporary acupuncture practice and social needs. It was recommended that the evidence from patient-reported outcomes (PROs), such as HRQoL, be adopted in acupuncture clinical research.

The revised draft *Guidelines* prepared by the Korean delegation for clinical research on acupuncture were used as the basic document for discussion.

2.2.1 Overview

The discussion was devoted to the concepts expressed in the *Guidelines* and to creating a sample outline for the revised draft, while maintaining the basic structure of the 1995 edition. However, the *Guidelines* were reorganized through amendments and additions to texts, terms, and position of indexes.

The first day involved 11 presentations that focused on a variety of specific issues related to acupuncture research and design of clinical trials. Following each presentation, there was an opportunity for questions and further discussion. At the completion of the day, an agenda for the following day was developed. On day two, the 14 temporary advisers were divided into three groups to discuss and revise three specific segments of the *Guidelines*. A draft template, developed by the Korean delegation, was used to guide the group discussions and the revision process. This process was supported by the WHO secretariat, who supplied word processing and electronic versions of the first edition of the *Guidelines* for modification. Lively discussion took place within the three groups, who reported back to the larger group later in the afternoon.

2.2.1.1 Group 1

The group was composed of Professors Sung-Keel Kang, Ikuro Wakayama, Nguyen Tai Thu, Se-Hyun Kim and Brenda Golianu. They were charged with revision of the following sections: "1. Introduction - including background, research on acupuncture, need for revised guidelines for the clinical evaluation for acupuncture and clinical research"; "2. Glossary"; "3. Goals and objectives of the guidelines"; and "4. General considerations - including legal considerations, ethical approval-

institutional review board, consideration of the character of acupuncture, clinical research, aims and selection of research projects, laboratory and clinical imaging studies, and education". In addition, the group also discussed section "5.7. Other considerations - utilization of medical classics, medicoanthropological studies, health-related quality of life, special population and new research strategies", "5.8. Conclusions", and "6. Using the guidelines". The discussions resulted in updates to the text, with additions and amendments.

2.2.1.2 Group 2

Professors Tat-Leang Lee, Liu Baoyan, Kenji Kawakita, Hi-Joon Park, and Peter White participated in group 2 discussions. The group sought to revise and amend the guidelines listed under section "5. Research methodology - literature review, systematic review and meta-analysis, treatment protocol, research team, and clinical research design". The clinical research design consists of the research question, acupuncture rationale and study design. The group discussed intervention studies-RCT under study design. RCTs consist of selection of subjects, sample size and power, research site, randomization, blinding, control, crossover trials, factorial design, sequential trial design, N-of-1 trials, and outcomes. Regarded as the 'gold standard', RCTs need to be discussed thoroughly from various perspectives. All amendments and additions were noted and a new document was compiled. This was then amalgamated into the main document.

2.2.1.3 Group 3

Group 3 was composed of Professors Hitoshi Yamashita, Liu Zhishun, Jung-Chul Seo and Christopher Zaslowski. The group sought to revise information on research designs besides RCTs. The discussion covered sections "5.5.3.2. Observational study (analytical studies such as cohort studies and case control studies, and descriptive studies such as cross-sectional studies and case series" and "5.5.4. Need for a multiphase approach", to "5.6. Administration and conduct of clinical research - protocol development, case report forms, data management, statistical analysis, monitoring of studies, reporting, and integration into evidence-based practice". Study designs other than RCTs are also important in clinical trials. Several sections were amended and new text added.

At the end of day two and on day three, all groups reconvened to discuss their draft amendments. All the revised proposals from the three groups were reviewed until a consensus was reached. All agreed that the goals of the meeting had been achieved.

2.2.2 Specific issues

The issues covered during the discussion included:

(1) Ethics:

The definition of new terms, such as Institutional Review Board (IRB) in the section on ethical approval was considered.

(2) Research methodology:

(a) Insertion of "systematic review and meta-analysis" in guidelines for clinical evaluation;

(b) Reorganization of clinical research design:

5.5. Clinical research design:

5.5.1. Research question;

5.5.2. Acupuncture rationale;

5.5.3. Study design:

5.5.3.1. Intervention studies – RCT;

5.5.3.2. Observational studies - analytical studies (cohort studies and case control studies) and descriptive studies (cross-sectional studies and case series);

5.6. Administration and conduct of clinical research;

5.7. Other considerations.

(c) Revision and updating of contents (e.g., classification of control groups as invasive needle control, dummy needling control, non-acupuncture-like placebo control, and pragmatic trials, etc);

(d) Adding new research designs (e.g., factorial design, cross-sectional studies, case series, qualitative studies, etc); and

(e) Addressing the need for a multiphase approach.

(3) Outcome measures:

Evidence-based medicine is very important and should form the basis for future acupuncture practice. However, the 'evidence' should also include the patient's perspective and such measures as HRQoL, qualitative studies, etc. need to continue to inform and influence the delivery of care.

(4) Conducting clinical trials:

A new chapter, "Administration and conduct of clinical research" to enable researchers to conduct better clinical trials, was introduced.

(5) Other considerations:

The practice of acupuncture has many unique features and research needs to defer to this. While the 'rigid' RCT is recognized as the gold standard, researchers need to be flexible and innovative in adapting various study designs to allow accurate assessment of contemporary acupuncture practice. The pragmatic trial is one method by which this can be addressed.

(6) Terminology:

One of the major problems that beset acupuncture research and its interpretation has been the variety of different control interventions and their terminology. The meeting identified several hitherto confusing terms and replaced them with a simpler method of classification.

The group agreed that a glossary with working definitions (e.g. IRB, HRQoL, invasive needle control, and dummy needling control, and non-acupuncture-like placebo control, CONSORT, STRICTA, etc) would be included in the revised *Guidelines*.

2.3 Field visit

The members of the Working Group visited the East-West Medical Research Institute, Kyung Hee Oriental Medical Hospital and Kyung Hee University in Seoul.

2.4 Closing ceremony

Dr S.H. Choi, Regional Adviser in Traditional Medicine, WHO Regional Office for the Western Pacific, pointed out in his closing remarks that the revised *Guidelines* would guide and enhance scientific clinical research on acupuncture. He indicated that the main theme of the traditional medicine programme in the WHO Western Pacific Regional Office is "Standardization with evidence-based approaches", and highlighted that revision of the *Guidelines for Clinical Research on Acupuncture* is one of the main steps to realize that theme, along with the standardization of acupuncture point locations, which is ongoing. He expressed his deepest appreciation to the Korean Experts Group for their great effort in preparing the draft revised *Guidelines*, and to the East-West Medical Research Institute of Kyung Hee University, which provided the financial support and hospitality for the meeting.

On behalf of all participants, Dr Peter White acknowledged the effort and support of the WHO Regional Office for the Western Pacific and the East-West Medical Research Institute, East-West Medical Center, Kyung Hee University, in holding the Working Group meeting and in developing the revised *Guidelines for Clinical Research on Acupuncture*. He also acknowledged the hospitality of the Association of Korean Oriental Medicine.

3. CONCLUSIONS AND RECOMMENDATIONS

3.1 Conclusions

- (1) It is hoped that the guidelines have captured the current state of knowledge on acupuncture research and provide a framework for initiating future projects.
- (2) Evidence-based medicine is very important and should form the basis for future acupuncture practice. However the 'evidence' should also include the patient's perspective and measures such as HRQoL, qualitative studies etc. need to continue to inform and influence the delivery of care.
- (3) The practice of acupuncture has many unique features and research needs to defer to this. Whilst the 'rigid' RCT is recognized as the gold standard, researchers need to be flexible and innovative in adapting the study design to allow accurate assessment of contemporary acupuncture practice. It is anticipated that this will aid the researcher in accurately reporting the study and enable the reader to better interpret the results.
- (5) Publication and dissemination of the revised *Guidelines* will promote better understanding and facilitate better communication between all interested parties. It is hoped

that this will produce quality research, enhance the practice of acupuncture, and improve patient health care.

3.2 Recommendations

In order to enhance the practice of acupuncture research, the following recommendations are proposed:

- (1) The use of standard WHO acupuncture nomenclature should be encouraged.
- (2) New nomenclature should be adopted with regard to controls and should be used in the study protocols, thereby assisting in standardization of reporting.
- (3) WHO should encourage journal editors to adopt WHO nomenclature.
- (4) The revised *Guidelines* should be disseminated in hard copy and made available electronically to enable worldwide access.
- (5) WHO should encourage Member States to translate the *Guidelines* into their native languages.
- (6) WHO should assist in the dissemination of research findings and their integration into clinical practice (in line with evidence-based medicine).
- (7) WHO should encourage journal editors to publish protocols and preliminary studies. In addition, they should provide space for complex trials to adequately report their methodologies.
- (8) WHO should encourage courses and training programmes in acupuncture research methodology to ensure the quality of future trials.
- (9) WHO should encourage education for health professionals in acupuncture terminology, practice and research.
- (10) WHO should encourage further dialog around the *Guidelines* within the home institutions of the participants and other interested parties in order to encourage their application and adaptation.
- (11) WHO should encourage Member States to translate and publish important clinical findings into other Member States' languages.
- (12) WHO should establish international networks and collaborative studies among clinical researchers in acupuncture, thus encouraging the development of high quality clinical trials. In this way, evidence-based practice will be facilitated and health care improved.

LIST OF TEMPORARY ADVISERS, OBSERVERS AND SECRETARIAT

1. TEMPORARY ADVISERS

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**SPEECH AT THE OPENING OF THE MEETING ON THE REVISION OF
GUIDELINES FOR CLINICAL RESEARCH ON ACUPUNCTURE
BY DR CHOI SEUNG-HOON, REGIONAL ADVISER IN TRADITIONAL MEDICINE,
ON BEHALF OF DR SHIGERU OMI, REGIONAL DIRECTOR,
WHO WESTERN PACIFIC REGION
24 AUGUST 2005
SEOUL, REPUBLIC OF KOREA**

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PROFESSOR LEE BONG-AM,

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DIRECTOR OF THE EAST-WEST MEDICAL RESEARCH INSTITUTE,
PROFESSOR CHO BYUNG-SOO,

DISTINGUISHED PARTICIPANTS, LADIES AND GENTLEMEN,

I am very pleased to welcome you all to the Meeting on the Revision of Guidelines for Clinical Research on Acupuncture. On behalf of the World Health Organization, I would like to express my sincere appreciation to the East-West Medical Research Institute, Kyung Hee University, for organizing the meeting as one of the WHO collaborating centres for traditional medicine.

Traditional medicine has been practised for thousands of years. It was the only available method of health care in this part of the world before Western medicine was introduced to Asia. Herbal medicines and acupuncture have long been the main pillars of traditional medicine in our Region. In this regard, in 1985 and 1987, the WHO Regional Committee for the Western Pacific adopted resolutions supporting the proper use of herbal medicines and acupuncture.

With the remarkable expansion in the use of acupuncture worldwide, safety and efficacy have become important concerns for practitioners, researchers and the public. The challenge has been to ensure that acupuncture is used properly and to determine how research and evaluation of acupuncture should be carried out. There have been increasing demands for WHO to provide standards, technical guidance and information on these issues.

In June 1994, a Working Group organized by the WHO Regional Office for the Western Pacific met in Aomori, Japan, to develop guidelines for clinical research on acupuncture. This represented efforts to introduce basic principles and methods used in modern scientific research to evaluate the effectiveness of acupuncture. In 1995, the Working Group unveiled its *Guidelines for Clinical Research on Acupuncture*.

The guidelines attempted to incorporate a broad range of issues and disciplines involved in clinical research on acupuncture and to be suitable for use by researchers engaged in many different areas related to the evaluation of acupuncture's effectiveness in treating various diseases and disorders.

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During the last decade, there have been hundreds of clinical studies on acupuncture. Some of them are included in the Cochrane Database of Systematic Reviews. It was proven that the guidelines furthered clinical research but at the same time, they were not sufficient to overcome the demanding issues in the clinical research on acupuncture.

There is a saying, "Ten years can bring a lot of changes." We are living in the age of change. The clinical research on acupuncture is not an exception. What is more, in the last decade, there have been numerous interdisciplinary studies in the acupuncture field with Western modern studies. Now is the time when we should update and compile those accomplishments. That's why we are here today from many parts of the world.

Lastly, I would like to express, on behalf of the World Health Organization, our sincere gratitude to those attending this meeting and our congratulations to the organizers on its auspicious opening.

Ladies and gentlemen, I wish you all a fruitful and successful meeting and an enjoyable stay in Seoul.

Thank you.

THE SCIENTIFIC BASIS OF ACUPUNCTURE

The ten years since the publication of these guidelines have seen innumerable studies published on acupuncture all over the world. A detailed summary of these papers is not possible. Rather, this section will aim to briefly summarize the main theories and hypotheses relating to the mechanism of action of acupuncture from a Western scientific viewpoint.

The anatomical correlation of meridians or acupuncture channels remains controversial. Although points are often located near major nerves, blood vessels or lymphatic vessels no channel correlates solely to any of these structures. With regard to the acupuncture point itself, it would appear that there is probably not simply one single anatomical structure but rather many, which together form a functional acupuncture point. The presence of a transdermal electrical potential has been well established and the acupuncture point, being of low resistance, may represent a short circuit in this system. Lastly, a wave of contraction has been observed to be transmitted between points via ultrasound. It would seem therefore that there may be several types of acupuncture points, with varying anatomical structures and various functions.

Mechanisms of Action Involved in Acupuncture

The mechanism of action of acupuncture from a Western scientific viewpoint has yet to be uncovered. It would seem likely however that for pain, there are several mechanisms through which this modality may work.

It would appear that the majority of studies point to the nervous system as being of prime importance in the mechanism of action of acupuncture. Indeed complete denervation completely suppresses the effects of acupuncture regardless of the other supporting structures such as blood vessels, muscles, etc. Functional magnetic resonance imaging studies suggest changes in blood flow in limbic and other brain structures following acupuncture.

In the management of painful conditions, segmental inhibition may play a role in localized pain relief. The need for an intact nervous system may also implicate both the pain gate theory of Melzack and diffuse noxious inhibitory control (DNIC) as being instrumental in the workings of acupuncture. Briefly, pain gate theory suggests that cells within the dorsal horn of the spinal cord, namely the substantia gelatinosa, act rather like a switch between afferent nerve impulses from different fibres. Slow (chronic) pain is carried by small unmyelinated C fibres, however when there is a preponderance of signals from other myelinated fibres such as A beta and A delta (responsible for touch, vibration and fast pain), the gate closes to C fibre impulses and allows the A fibre signals through. Descending inhibition mechanisms in the spinal cord may also play a role.

Segmental effects do not however explain the effects of acupuncture seen throughout the body. Endorphin release has been demonstrated in the brain with low frequency stimulation while high frequency stimulation releases dynorphin. The effects of acupuncture are only partially reversed by systemic naloxone suggesting not only an opioid involvement but other systems as well. Release of over 20 neurotransmitters has been associated with acupuncture treatment.

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Another possible mechanism which may explain the non-segmental effects of acupuncture, is that of DNIC (Le Bars et al. 1991). The dorsal horn neurons are inhibited by a nociceptive afferent signal applied to any other part of the body. Therefore any applied painful or noxious stimulus (such as an acupuncture needle) will attenuate existing pain even in extra-segmental areas. It is suggested that this works by both peripheral and central systems. The peripheral system works via A delta and C fibres and indeed the propagation of 'deqi' may be a sign of activation of the A delta fibres (Andersson 1993). If this sensation is blocked by the local injection of procaine, acupuncture is ineffective. The central mechanism is via descending inhibition from brainstem structures such as the Nucleus Raphe Magnus. In support of the involvement of 'higher' structures in this aspect of pain control is the fact that stimulation of the para-aqueductal grey (PAG) in the midbrain will inhibit responses of the spinal cord neurons to noxious stimuli. It is also suggested that endogenous opioids may participate in the DNIC mechanism.

A positive relationship between serotonin levels and the effectiveness of acupuncture would also tend to implicate this substance in the mechanism. Similarly, serotonin levels tend to increase after acupuncture if the treatment has been effective. It has also been noted that acupuncture tends to be less effective when used on depressed patients and there may therefore be a link between decreased levels of serotonin in these patients and failure of acupuncture to achieve good pain relief. The sympathetic and parasympathetic nervous systems may also be involved.

Lastly, insertion of an acupuncture needle may similarly cause a change in the endogenous electrical fields within the body which in turn may have an effect on the tissues nearby and may even serve to correct a homeostatic imbalance.

It would seem therefore that acupuncture works through a series of mechanisms including segmental reflexes, electrical, vascular and neural. Continued work into the nature of these mechanisms and to identify the precise manner in which these mechanisms work together will inform further clinical research efforts.

References

- Andersson S. 1993. "The functional background in acupuncture effects". *Scand. J. Rehabil. Med. Suppl.*, vol. 29, SGH.
- Becker R. 1974. "The significance of bioelectric potentials". *Bioelectrochemistry and Bioenergetics*, vol. 1, pp. 187-199.
- Bensoussan A. 1994. "Part 1: Acupuncture meridians - myth or reality?", *Complementary Therapies in Medicine*, vol. 2, no. 1, pp. 21-26.
- Bing Z., Villanueva L., and Le Bars D. 1990. "Acupuncture and diffuse noxious inhibitory controls: naloxone-reversible depression of activities of trigeminal convergent neurons", *Neuroscience*, vol. 37, no. 3, pp. 809-818.
- Bossy J. 1984. "Morphological data concerning the acupuncture points and channel network", *Acupunct. Electrother. Res.*, vol. 9, no. 2, pp. 79-106.
- British Medical Journal. 2000. 321(7262): 694-696.
- Chan S.H. 1984, "What is being stimulated in acupuncture: evaluation of the existence of a specific substrate", *Neurosci. Biobehav. Rev.*, vol. 8, no. 1, pp. 25-33.
- Chernyak G.V., Sessler D.I. 2005. Perioperative Acupuncture and Related Techniques. *Anesthesiology*, vol. 102, pp. 1031-49.
- Ciszek M., Szopinski J., and Skrzypulec V. 1985. Investigations of morphological structure of acupuncture points and meridians. *J. Traditional Chin. Med.*, vol. 5, pp. 4:289-292.
- Edelberg R. et al. 1960. "Some membrane properties of the effector in the galvanic skin response", *J. of Applied Physiology*, vol. 15, pp. 691-696.
- Han J.S. 2004. Acupuncture and endorphins. *Neurosci. Lett.*, vol. 361 (1-3), pp. 258-61.
- Heine H. 1988. "Anatomical structure of acupoints", *J. Traditional Chin. Med.*, vol. 8, no. 3, pp. 207-212.
- Lazorthes Y., Esquerre J.P., Simon J., Guiraud G., and Guiraud R. 1990. "Acupuncture meridians and radiotracers", *Pain*, vol. 40, no. 1, pp. 109-112.
- Le Bars D., Villanueva L., Willer J., and Bouhassira D. 1991. "Diffuse Noxious Inhibitory Controls (DNIC) in Animals and Man", *Acupuncture in Medicine*, vol. 9, no. 2, pp. 47-56.
- Lewith G.T., White P.J., Pariente J. 2005. Investigating Acupuncture Using Brain Imaging Techniques: The Current State of Play. *Evidence-Based Complement Alternat. Med.*, vol. 2(3), pp. 315-319.
- Lewith G., Jonas W.B. and Walach H. (Eds). 2002. *Clinical Research in Complementary Therapies. Principles, Problems and Solutions*. Churchill Livingstone: Edinburgh.
- MacPherson H., White A., Cummings M., Jobst K., Rose K. and Neimtzow R. 2002. Standards for Reporting Interventions in Controlled Trials of Acupuncture: The STRICTA recommendation. *Acupuncture in Medicine*, 20, 22-25.
- Melzack R. 1981. "Myofascial trigger points: relation to acupuncture and mechanisms of pain". *Arch. Phys. Med. Rehabil.*, vol. 62, no. 3, pp. 114-117.
- Moher D., Schultz K. and Altman G. 2001. The CONSORT Statement: Revised recommendations for improving the quality of reports of parallel group randomized trials. *The Lancet*, 357, 1191-1194.
- Murray J.B. 1995. "Evidence for acupuncture's analgesic effectiveness and proposals for the physiological mechanisms involved". *J. Psychol.*, vol. 129, no. 4, pp. 443-461.
- Fayers P.M. and Hays R.D. 2005. *Assessing Quality of Life in Clinical Trials*. Oxford: Oxford.
- Salzberg C., Miller A., and Johnson L.K. 1995. "Acupuncture: history, clinical uses, and proposed physiology", *Physical Medicine and Rehabilitation Clinics of North America*, vol. 6, no. 4, pp. 905-916.

Annex 3

- Sims J. 1997. "The mechanism of acupuncture analgesia: a review", *Complementary Therapies in Medicine*, vol. 5, no. 2, pp. 102-111.
- Stux G. and Pomeranz B. 1995. "Basics of acupuncture", *Springer-Verlag New York*, 309 p).
- Stux G. and Hammerschlag R. (Eds). 2001. *Clinical Acupuncture. Scientific Basis*. Springer Verlag: Berlin.
- White P. 2004. Methodological Concerns when Designing Trials for the Efficacy of Acupuncture Treatment of Pain. In Cooper E. and Yamaguchi N. (Eds). *Complementary and Alternative Approached to Biomedicine*, p. 217-227. New York: Kluwer Academic Publishers.
- Wu D.Z. 1990. "Acupuncture and neurophysiology", *Clin. Neurol. Neurosurg.*, vol. 92, no. 1, pp. 13-25.
- 고응린 (Go, U.R.), 임상시험과 자료분석 (Clinical trials and data analysis). 신광출판사 (ShinKwang publishing company), Seoul, 2002.
- 김영설 (Kim, Y.S.), 증거의학을 위한 임상의학연구방법론 (Clinical medical research methodology for the evidence-based medicine), Seoul, 2003.
- 신양규 (Shin, Y.G.), 한의학 연구를 위한 통계적 방법 (Statistical Methodology for Oriental Medical Research). 경산대학교 출판부 (Kyungsan University Press), Kyungsan, 2003.
- 신영수 (Shin, Y.S.), 안윤옥 (Ahn, Y.O.). 의학연구방법론 (Medical Research Methodology), 서울대학교 출판부 (Seoul National University Press), Seoul, 1997.

REVISED GUIDELINES ON CLINICAL RESEARCH ON ACUPUNCTURE

FOREWORD

It has been 10 years since the first publication of *Guidelines for clinical research on acupuncture* in 1995. During this time there has been increased interest in acupuncture research and the number of published acupuncture research studies promotes further discussion and research activities. Consequently, there is a need to update the recommended guidelines to keep abreast of new developments in research methodologies.

More evidence-based studies in clinical acupuncture are needed, while always keeping in mind the benefit and safety to the patients being treated. At the same time, we have to consider that newly developed clinical research methodologies on acupuncture should properly reflect the true essence of acupuncture treatment, which has been used for more than two thousand years in our Region.

In this regard, it is hoped that these guidelines will promote continued development of clinical researches on acupuncture and facilitate its use in the global environment.

Shigeru Omi, MD, Ph.D.
Regional Director

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1. INTRODUCTION

1.1 Background

Acupuncture has been applied as a therapeutic medical technique in China for more than 2500 years although its development goes back further. In the 2nd and 3rd century BC, the theory of acupuncture was already well developed as shown in the writings of the *Huangdi Neijing* (The Yellow Emperor's Internal Classic). Acupuncture, a simple and effective clinical procedure, was introduced in the Republic of Korea, Japan and Viet Nam in the 6th century. In the early 16th century, acupuncture came to Europe and in the 19th century to North America.

During the last two decades, acupuncture has continued to spread worldwide. There has been growing interest in the therapeutic applications of acupuncture, and a desire to explain its modes of action in terms of modern scientific knowledge. WHO has been aware of the potential value of acupuncture and its possible contribution to WHO's goal of 'health for all'.

In 1985, the Regional Committee for the Western Pacific adopted a resolution on traditional medicine which recognized that traditional medicine practices, particularly those of herbal medicine and acupuncture, constitute appropriate therapies that could be integrated into national health strategies. The resolution urged Member States to initiate programmes of research, training and information.

In 1987, another resolution was adopted by the Regional Committee. This resolution reiterated the value of herbal medicine and acupuncture and strongly supported Member States to establish or further develop programmes on traditional medicine, particularly herbal medicine and acupuncture, in the light of their specific needs and circumstances.

Concurrently, the Regional Office for the Western Pacific identified that about one third of acupuncture point locations were controversial among the Member States and initiated a standardization of the acupuncture point locations. It is expected that the standard of acupuncture point locations will provide the firm basis of reliable clinical research on acupuncture.

1.2 Research on acupuncture

Acupuncture is recognized throughout the world as a valuable and readily available resource for health care. The practice of acupuncture is rooted in the tradition and personal experience of many generations of traditional practitioners in many countries. Although acupuncture has been used for thousands of years, appropriate evidence-based studies are needed to supplement its rational use and further development.

In the performance of clinical studies, investigators should evaluate clinical efficacy and outcome measures. Additional studies should also attempt to investigate mechanisms of action. Research teams should prioritize clinical effectiveness over mechanistic studies as this is directly concerned with promotion of health and health care delivery.

1.3 Need for revised guidelines for the clinical evaluation of acupuncture

Clinical studies and related research are being undertaken in many countries. There is a need for scientifically rigorous approaches and methodologies in order to facilitate comparison and reproducibility of results. Application of basic principles and methodology of modern science, e.g. design, conduct, statistical analysis, interpretation and reporting, must be understood and applied by acupuncture researchers. In 1989, a WHO scientific committee, which met in Geneva, recommended that WHO play a role in consolidating guidelines on research methodology to ensure the acceptable quality of results. The purpose of revising the guidelines is to update and enhance the previous recommendations so that the scientific basis of acupuncture practice can be further enhanced and developed.

1.4 Clinical research

Clinical research is performed to allow:

- (1) the patient to make clearer decisions about treatment options;
- (2) the practitioner to be better informed on effectiveness and efficacy; and
- (3) health policy and funding authorities to make appropriate decisions about utility and cost-effectiveness.

The purpose of clinical acupuncture research is therefore:

- (1) to allow the patient to make decisions based on effectiveness (absolute and relative), safety, cost, relationship with concomitant conventional care, cultural factors and patient preference; and
- (2) to develop guidelines for good clinical practice for acupuncturists.

A similar agenda exists for both the practitioner and the health funding organization (change as needed according to subsequent list). This should lead to the rational use of acupuncture.

The methods of clinical research available include:

- (1) randomized controlled trials (RCTs)
- (2) cohort studies
- (3) case control studies
- (4) cross-sectional studies
- (5) case series
- (6) sequential trial design
- (7) n of 1 trials
- (8) qualitative studies.

A clinical trial is defined as a scientific experiment involving human subjects in which treatment is evaluated.

The conduct of clinical trials is governed by the underlying purpose of the study and is therefore directly related to the outcome. A clinical trial has three fundamental components:

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- (1) data collection
- (2) evaluation design, such as RCTs, cohort studies, case control studies, etc.
- (3) outcome.

When outcome is used as a measurement for evaluation purposes, it is usually called "endpoint". The validity and reliability of endpoints always have to be considered. The study of cost-effectiveness and cost-utility will be conducted utilizing these data.

RCTs, as a "gold standard" in various methods of clinical trial, can be used to answer questions about most clinical problems. However, this approach is not always a practical and cost-effective solution. Pragmatic trials that do not "unpack" all the treatment options may therefore be required.

2. GOAL AND OBJECTIVES OF THE GUIDELINES

2.1 Goal

The goal of the guidelines is to promote ethical design and conduct of acupuncture clinical research.

2.2 Objectives

The objectives are:

- (1) to provide basic principles and applicable standards for researchers and acupuncture practitioners to prepare and conduct clinical studies on the therapeutic value of acupuncture;
- (2) to facilitate the exchange of research findings and other information so that a body of reliable data for the validation of acupuncture can be accumulated; and
- (3) to provide standardized acupuncture research terminology.

3. GENERAL CONSIDERATIONS

3.1 Legal considerations

Governments should actively encourage research on acupuncture, particularly clinical evaluation, as well-designed research will facilitate evidence-based practice and therefore improve health care delivery.

Legislation on acupuncture and regulation of acupuncture practice can play an important role in assuring the quality of acupuncture service and administration of acupuncture practice.

3.2 Ethics approval

The study protocol should be approved by an institutional review board (IRB). The IRB will generally be established at an institutional level, but boards existing at a regional or national level can also be consulted. The IRB will be an independent body made up of both medical and non-medical members who are not involved in the study under review. The IRB will protect the rights and welfare of participants and ensure the research has merit and integrity. The work of the board should be guided by the Helsinki Declaration and other related documents prepared by the individual country or institutions.

3.3 Consideration of the character of acupuncture

Acupuncture was developed as a branch of traditional medicine on the basis of oriental philosophy. This philosophy takes a holistic approach to regulating the balance of the human body. The existence of several different traditions gives rise to a diversity of practice.

A good clinical study on acupuncture should be conducted with the understanding and integration of both traditional and/or modern knowledge of medicine. As much as possible diagnostic criteria for both traditional and western medicine should be used.

3.4 Clinical research

3.4.1 Aims

Acupuncture may be used as:

- (1) a therapeutic intervention including rehabilitation; and
- (2) a preventive and health maintenance intervention.

Clinical research in acupuncture may also benefit other health professionals and the scientific community, as acupuncture research may provide important heuristics for their practice.

3.4.2 Selection of research studies

Research studies should, in addition to scientific interest, address local needs and aim to improve the general health of the community. The scientific acceptability of the study should be considered. Studies may explore outcomes of traditional techniques, or mechanisms of action underlying traditional methods. They may also be conducted to validate new acupuncture treatments. A comparative study on the therapeutic value of different points, various needling techniques, may also be conducted.

3.5 Laboratory and clinical imaging studies

Related laboratory and clinical imaging studies will provide data that will inform mechanisms of action.

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3.6 Education

Dissemination of knowledge about acupuncture and acupuncture research to professional health workers can greatly aid the overall efforts to improve the clinical evaluation of acupuncture.

The general public will also benefit from adequate information on the clinical effects of acupuncture and the outcome of clinical research.

4. RESEARCH METHODOLOGY

4.1 Literature review

As acupuncture was developed before the advent of modern science, is based on a different culture and philosophy, and has only recently been investigated scientifically, it must be recognized that some knowledge about acupuncture is to be found in anecdotal observations or case reports. Furthermore, it must also be recognized that while some early publications on acupuncture may not meet the stringent requirements, they may still provide potentially useful observations and ideas for further study. However, the need for a solid scientific foundation is also recognized, and so greater weight should be attached to evidence drawn from rigorous RCTs. Therefore, a thorough literature review should be carried out for the clinical evaluation of acupuncture.

4.2 Systematic review and meta-analysis

A systematic review is a detailed review and analysis of previously published literature to answer clearly formulated questions. It uses systematic and explicit methods to identify, select and critically appraise relevant research, and to collect and analyse data from studies that are included in the review.

To minimize bias and random errors, literature from multiple sources is systematically and thoroughly searched for, assessed and evaluated. The evaluation must take into account:

- only acupuncture trials;
- the nature and appropriateness of the treatment used for each selected trial;
- the homogeneity of condition reviewed; and
- the overall scientific quality of each trial, including any factor that might introduce bias and/or confounding (e.g. the control used and the internal and external validity).

Meta-analysis should be carried out where appropriate. A large number of acupuncture systematic reviews exist that suggests there is a need for well-designed, larger clinical trials.

4.3 Treatment protocol

To ensure the reproducibility of a clinical study on acupuncture, related acupuncture treatment should be clearly presented and exact protocols should be established.

- The standard acupuncture nomenclature developed by the WHO Regional Office for the Western Pacific and recommended by WHO scientific group that met in Geneva in 1989 should be used during the study.
- Length and diameter of needle(s) should be given in millimetres (mm).
- For reliable locations of acupuncture points, the use of International Standard of Acupuncture Points Locations established by the WHO Regional Office for the Western Pacific should be encouraged.
- Needling techniques of insertion, stimulation, retention time and withdrawal should be standardized and stated in the protocol. All efforts for standardizing the individual influence of investigators on the performance of the needling technique should be considered.
- As a treatment regimen, the frequency of treatment, treatment duration and number of sessions should be clearly described.
- All concomitant treatments and co-interventions need to be clearly recorded and described, e.g. traditional or western medical interventions, lifestyle advice, sports exercise.
- The use of auxiliary acupuncture equipment such as lasers or electrical stimulators should be clearly described.
- Other factors related to the patient's condition, such as biorhythm, breathing and position, may also need to be reported.
- The use of STRICTA guidelines is recommended.

The use of pragmatic trials has gained a certain amount of momentum in acupuncture research. This is because the treatment follows normal, everyday practice, i.e. a 'pragmatic' regime. Thus individualization of treatment is assured. The disadvantage of this technique is that the trial loses "generalizability" because the results are less reproducible due to practitioner variability.

4.4 Research team

The research team involved in the study should have appropriate expertise, qualifications and competence to undertake a study. It is recommended that a team should comprise acupuncture practitioners, statisticians, scientists and professional health workers. Knowledge of both acupuncture and the specialist field, which is needed to evaluate the effectiveness of acupuncture, will be required for preparing and conducting a rigorous clinical study.

The research team is responsible for the trial and for the rights, health and welfare of the subjects in the trial.

The research team must be aware of the following responsibilities:

- (1) appropriate and ongoing care of patients in the study;
- (2) ethical requirements for the study (for instance the need to terminate protocol treatment if the patient is harmed or at risk by continuation of the study);
- (3) knowledge of acupuncture; and
- (4) an appreciation of research methodology.