REGIONAL PERSPECTIVES IN HUMAN GENETICS
I. INTRODUCTION

The new discoveries and knowledge of gained in human genetics and related biology in recent decades as well as the potential of having newer understanding and exploration have raised the expectations as well as many scientific applications for making a significant improvement in human health. If such discoveries, knowledge and technology gained are integrated into the health care systems in ethically, socially, economically and legally accepted ways, the increased benefits for diagnosis, prevention, promotion and treatment of many diseases, including human genetic conditions will be greatly appreciable in both developed and developing world.

The topic of human genetics became more prominent in recent years as a subject of public health, biology and social science, legal and medical interests, due to the advancement of the work of the “Human Genome Project” (HGP), which is a global multinational and multi-corporate scientific effort started in 1988. The development on human genetics has started almost a century ago, from classical genetics, reverse genetics, genomics, proteomics, and to new genetics. It may likely move into the era of new science of biomics.

With the advancement of biotechnology, bioinformatics, computational biology and other sciences including engineering and industrial applications, the understanding of human genetics and genomes has become much more clearer. It gives a new wave of development of biology and biomedicine, leading to new ways of prevention and control of many diseases including genetic-related diseases both for individuals, relatives and populations in larger scale.

WHO is working closely with all scientific partners in the development of appropriate guidelines and training with respect to the Ethical, Legal and Social Implications (ELSI) of human genetics and genomes for some decades. Around the time when the first phase of HGP completed in 1998, WHO has produced an international guide proposed for use by all scientists, viz., “Proposed international guidelines on ethical issues in medical genetics and genetic services”. Since then, a series of scientific debates as well as national and international actions on human genetics have been carried out. Masses of international committees, commissions, advisory bodies and many reports, research papers and national and international guidelines have been produced on various issues and aspects of development of human genetics. At the same time, there is a rapid advancement of the Human Genome Project for completing its tasks.

Because of these rapid developments in the area of human genetics with possible implications of how these advancements could help to improve the health of the poor, WHO Director-General has requested the Global Advisory Committee on Health Research (ACHR) to prepare a special report on the Genomics and Health. Concurrently, WHO Regional Director for South-East Asia also requested the SEA Regional ACHR to undertake a scientific debate at its 26th session; and to make advise through him to Member
Countries on regional perspectives of human genetics, especially ethical, legal and social implications (ELSI), which may be crucial to full utilization of scientific development.

This working paper is prepared with the objective of providing brief accounts of development of human genetics and ELSI implications, and possible areas of debate in order to solicit future strategic directions and actions to be undertaken.

II. BACKGROUND

The human body is made up of a hundred million cells of various types. Each contains the inherited information that comes from a single cell following fertilization. This information is packaged in the form of genes made up of DNA. The complete collection of gene, which is called genome, is a set of instructions for constructing human being. It is estimated that the entire human genome consists of 50,000 to 100,00 genes.

Since the beginning of the work on human genetics in 18th century, the development can be categorized by a few historical eras. The first era was the classical genetics where phenotypes of interest among family members are observed to identify segregation patterns of the “functional units” of genes or different forms of gene (alleles) and to lead to understanding of genetic mechanisms of particular phenotypes. Up to the mid-1900s, there has been a wide belief that nothing can be done for inherited diseases. With the discovery of DNA in 1953 and when physical mapping of genes on chromosome came into stage through the rapid progress in molecular genetics with recombinant DNA technology, in the next few decades, the era of new genetics emerged. The invention in physical mapping and gene sequencing has made the prevention and treatment of genetic disorders possible. In this reverse genetics era, there is a reverse of the work from classical genetics by which the scientists worked backwards from the genes to the phenotypes.

The human genome project (HGP) started in 1988 is to make genetic map and sequencing of human genes and other organisms. Knowledge derived from human genome mapping and related analytical and technological development would permit improved methods for diagnosis, intervention and prevention of diseases with genetic predisposition such as cancer, coronary heart diseases and of diseases caused by infections and other environmental agents. Examples of the impact on medicine and public health of the advances of human genetics mapping include the discovery of: dystrophia gene leading to better diagnosis methods for carrier detection and prenatal diseases, cystic fibrosis gene leading to population screening programme, breast cancer genes leading to screening of family members at risk.

Genetic therapy is considered as a new strategy in the health care of individuals and populations. The discovery of new knowledge in human genetics would give rise of exploring new pharmaceuticals, which might
prevent people from developing diseases. With the potential of the human genomics to invent new ways in combating diseases through gene interventions, much hopes are put towards prioritizing diseases that affect most of the world population. The human genomics will bring a new perspective of genetics and will be one of the technological revolutions in the field of biology and medicine.

The development in human genetics including those of the human genome project has led to the tremendous implications for health with respect to ethical, legal and social aspects. While some issues have awakened, some will be cropping up. The preparations to deal with them will have to take place. A few questions arisen are: Whether people should be screened for disease genes? Would this cause unnecessary anxiety? Will some known carriers of disease genes take advantage of health insurance? Will insurance company raise premium for know carriers of serious diseases? Will carriers of certain disease-genes be discriminated against in job placement? Which genes can be patented and which should not? Should some techniques for screening for disease genes be made commercial? Etc.

Therefore, ethical, legal and social implications (ELSI) of human genetics have been the prime concerns of many countries. The fundamental understanding of life and health with possible interventions has improved and the conceptual thinking has changed from preventive medicine, to predictive medicine and later to precision medicine. The ELSI in human genetics development was envisaged when the HGP started and it was included as part of the project activities. The ELSI activities have later spread beyond the HGP.

The rapid development of human genetics and genomics in recent years and with the possible acceleration in near future will definitely bring revolution to human biology and health and its impact on the human society will be profound. It is not just for those people who are involved in biology and medical sciences have to be sensitized to the upcoming age of new genetics and its implications. There are wide arrays of people like politicians, planners, public health, clinical specialists, general practitioners, social scientists, legislators, religious leaders, ethicists, historians and also common people, who need to be oriented with ethical, legal, social and economic implications of new genetics. Wider public understanding will contribute to mobilizing political will as well as to strengthen society’s capacity to deal with the rapid development of human genetics and its application to health care. It is a challenge of national health research councils or similar analogous body to be in the main stream of revolution that would be brought about by the genomics.

III. ETHICAL, LEGAL AND SOCIAL IMPLICATIONS (ELSI)

Major issues of ELSI that are continuously debated for some years and that might require greater attention due to new challenges presented by rapid advances in human genetics and its applications are as follow.
**Cloning:** While the technological development in human genetics, especially cloning has made tremendous advances in biomedical sciences, especially for diagnostics, vaccines and other therapeutics. WHO has urged Member States not to accept cloning of human beings, and it was agreed universally that human cloning be condemned. While several arguments are given against human reproductive cloning, like liability to abuse, violation of individual’s right, allowing eugenic selection, etc., there are a number of arguments in favour, such as general liberty, individual’s right to freedom to make reproductive choices, treatment of infertility, etc.

**Genetic counseling:** It is a process by which patients/relatives at risk of a disorder that may be hereditary are advised of the consequences of the disorder, the probability of developing or transmitting it and the way that it might be prevented, avoided or ameliorated. The ethical, legal and social concerns may arise for individuals, their families and their physician when genetic information about a gene disorder is sought or used in a clinical context. Ethical aspects relate to voluntary use of genetic testing and screening and there shall be no compulsory provision of accurate and accessible information. Confidentiality must be ensured.

**Genetic Screening and Testing:** The screening of genes refers to testing offered to a population group to identify asymptomatic people at an increased risk from a particular disease or adverse outcome. Diagnostic testing of genetic diseases of an individual is done to analyze the status of a particular genetic problem, that a person might have developed or at risk of developing such problem. Main purpose of genetic screening or testing is to prevent disease or secure early diagnosis and treatment. In addition to the availability of testing or screening genetic disorders, most developing countries have not adequate health care facilities for proper counseling and prevention or treatment of cases once disorders identified.

**Gene detection** in addition to making diagnosis in individuals, more precise can be coupled with molecular epidemiology, which will contribute to improved clinical decision analysis. This will help patients care to be more effective.

**Pharmacogenetics:** There is currently great interest in the pharmaceutical and biotechnology industries in increasing both on knowledge and application of pharmacogenetics. The birth of pharmacogenetics as the genetic basis for individuality in response to drugs was brought in the end of the 19th century. In its development, the scientific advances identified that there are marked ethnic differences in the distribution of allele variants of many drug-metabolizing enzymes. Alleles, which are not present or are present at only very low frequencies in the Caucasian population, may be significant determinants of drug response in other populations, and
thus, making specific ethnic groups much more sensitive to a particular drug regimen. The knowledge of the genetic basis of individual in response to drugs is of significance clinical and economic importance and may provide the basis for rational drug prescription.

**Xenotransplantation**: Significant ethical issue will appear if organ transplantation becomes a clinical reality for the choice that unavoidably has to be made. Informed consent is also a problem with xenotransplantation, whether patient should be truly given the information, given the uncertainty, which surround the early trials and the obligation of the patient to undergo long term and continuing control for evidence of vital and other infections transmitted from the animal donor. The success of organ transplantation has led to an ever-increasing shortfall between the demand for organs and supply. This has led to extensive investigation of the possible use of animal especially the pig as organ donor. However, a number of major barriers to successful xenotransplantation exist in a number of areas such as immunological, physiological, anatomical infection and ethical problems and animal rights.

**Genetic analysis** will rely on the analysis of the DNA variation from large population base cohorts. These studies will provide important on population and disease genetics and have the potential to make significant impact in the current health care practices.

**Stored DNA, DNA banking** in tissue or blood samples or other human specimens may provide useful information for examination of genetic disorders in families or for biomedical research. The following issues need to be considered:(a) protection of individuals from possible discrimination by employers or insurance companies; (b) possible benefits to the individuals from research findings, including families of patients/donors having access to learn the results on their DNAs; and (c) possibility of multiple uses of same sample in different and unforeseen research projects. The legal concern deals with blanket informed consent, ownership of genetic materials, patenting and commercialization. Some countries have questioned the ethical and legal aspects on continuous happening of shipment of human cells, tissue and DNAs to the laboratories abroad for genetic investigations of one kind or another.

**Disclosure and confidentiality** issues are the most appearing problems in medical genetics. Genetic disease does not only affect the individuals, but also the close related members in the family and the relatives. The results of the genetic diagnosis have to be informed undue delay. However, the possibilities of harm from disclosure to institutional third parties made the information to be taken in utmost care to protect confidentiality.

**Research**: When it comes to the research methodology in human genetics, the most important ethical considerations are the informed
consent and confidentiality. These issues are obviously faced on genetic screening as well as genetic testing, which are mostly done at the prenatal stage of women.

Due to lack of the cases in the developed world, or strict country regulation which prohibits researchers to conduct the study in their own developed countries, trials and experiments have to be carried out or involving the developing countries.

The none-health issues in human genome research become obvious. This covers patent, intellectual property rights, code of conducts of north and south research on human genome relationship, - which are as important as the health issues itself. The US patent office has tentatively ruled that human DNA sequence can be patented and must involve indication of developing products to benefit human health. The purpose of patenting is to avoid commercial patenting. However, whether gene should be patented is another issue, because people belief that genes are a part of gift from God.

Centres for human genetics research: Although research on human genetics and human genome does attract scientists and researchers, little support can be obtained from the national authorities, due to the high cost of such projects and also giving the least priority of country’s health needs. To overcome the problems of resources, establishment of regional and national human genetics research centres that have already high resource investments, could be an alternative. These few centres could also be designated as WHO Collaborating Centres for human genetics. For utilization of research results, the centres are able to improve cooperation between public health authorities research bodies and medical institutions. The research agenda should be focused on biotechnology advances for the most prevalent diseases of the member countries

Eugenics: deal with the current practices of prenatal testing and genetic selection, which aim to reduce the numbers of people with genetic disorders. The key aspect of eugenics is the coercion of people's reproductive choices, for social ends, which may include improving the quality of population, preventing suffering of future generations or reducing financial cost of life. Many eugenicists, including the founder of the eugenic movement, Francis Galton, opposed to coercion, believing that if people were properly informed, they would naturally make the “right” reproductive decisions. The fear is with the social market forces in eugenics, which would result in predictable pregnancy outcomes. It is perhaps benefiting people who wish to avoid the birth of disabled children. But eugenics sets up a new relationship between parents and offspring. Children are likely to feel they are no longer gift from God or the random forces of nature, but rather a selected products exercising in part of the parents aspirations, desires and whims. Disable people may feel that free market eugenics will correspondingly lessen society's tolerance for those with congenital
and genetic disorders. In short, the key issue and the most difficult question lies for which conditions should be permissible for eugenics. Clearly there is a need for specific regulation in eugenics.

**Training:** Member countries in the Region cannot escape the implications and impact of advances in human genetics. It is priority that governments to make commitment and action plan to cultivate expertise in the area of human genetics. Training for scientists-biological, medical, physical, engineering, information technology and allied health personnel in light of current genome knowledge, is timely.

**Dissemination of information:** At the same time public concern about medical advances has increased. Responses in the media to new discoveries such as cloning of Dolly and Andy demonstrate how responsive people are but also how poorly these advances are often understood clearly. Starting educating people on the enormous discovery of the finalization of human genes has to go not just for public but also for the decision-makers, and planners. As important as the prior is the dissemination of information relates to the establishment of appropriate and reliable means for publishing the importance of human genome research, its applications and limitations.

**Public policy and policy development.** Genetic conditions occur with similar frequencies in different nations and irrespective to the socioeconomic status of individuals. A meaningful right to health care must include access to service for the diagnosis, treatment and prevention of genetic disorders. The priority assigned to genetic services with respect to other health services is a matter of public health policy in each country. The public policy on ELSI on human genetics therefore covers among others the proper use of genetic data and genetic counseling in a social cultural context and the intellectual property schemes relate to human genetics and genome research.

Policy development should relate to the privacy and fair use of genetic information particularly in health insurance, employment and medical research. Such policy developments and legal enactment become necessary because some health insurers or potential employers may seek access to results of genetic testing to screen individuals who could place a disproportionate cost burden on their economics. The information on genetic testing result therefore should be kept as private information.

In most developing countries, including those of the Region, not much concerted efforts have been made so far to deliberate on ELSI in the human genomics, specially taking into account the prevailing social, cultural, religious, economic, health care and legal systems. On the other hand, it is to admit that a number of member countries of the SEA region are quite well advanced in responding to biotechnology and medical advancement. The biotechnology and biomedical scientists and experts form various national institutions are engaged in
many international activities in biotechnology and human genetics. In the area of biomedical research as well as training in relation to human genetics, much have been accomplished.

**Regional Situation Analysis:** Due to diversities in strengths, challenges and potentials of countries in the Region in the field of human genetics, a regional situation analysis becomes as important as to identifying disease priorities. There is a need in identifying potential use of genetic technology and finding strategies to help focus new technology on the disease burden in SEA member countries.

**The role of WHO:** WHO is uniquely equipped to consider the new ethical issues that arise from the development in human genetics, by virtue of its mandate to pursue public goods and to assist all nations in efforts to improve health of the population. Therefore, WHO needs to continuously develop policies that will ensure that these applications can become accessible to all and are provided with due regards to ethics and justice worldwide.

WHO could also provide leadership in the national, regional and international debates on issues related to ELSI on human genetics, as well as the provision of medical genetic services. For the Region, SEARO can cater conferences to examine the implications for developing countries of advances in genetics and related biotechnology.

WHO is responsible for the development of regional guidelines on human genetics (more of operational nature such as counseling guidelines) and ethical guidelines, norms and standard for genetic testing and other health related gene technology setting according to the regional cultural context. Validation of authoritative source of information on human genetics and making it widely available is the job of WHO. In line is to facilitate the development of regional network for human genome research to create cooperation and technology transfer among member countries.

WHO can play advocacy role as to provide platform for consensus among SEA countries on issues dealing with consent, counseling, confidentiality, the usage of genetics information by employers and insurers, counseling readily available for those being genetically screened as well as being tested.

IV. POINTS FOR CONSIDERATIONS

Health research promotion and development is reviewed from time to time as part of health systems development. WHO South-East Asia Advisory Committee for Health Research (SEA-ACHR) is a mechanism at which the influence is made on the development of biomedical and social sciences,
research policy and research programme development. The ACHR members are represented from the national Medical Research Councils (MRCs) or the National Health Research Institutes (NHRI) who bear various technical expertise and discipline.

At the annual session of SEA-ACHR, the members usually reviewed the topic of interest of scientific and technological development that might have implications to health development of the Region. The debates usually came up with the advice on research policies and strategies and in some cases, implementation actions. The contents discussed in the meeting may vary from time to time, based on the uprising health problems among countries, the socioeconomic and political situations in member countries as well as the global changes and trends which have an effect toward the changes and trends of health research.

The 26th SEA-ACHR to be held in Bhutan from 17-20 April 2001 will have a debate on the human genetics and genomics as a topic that has been brought into concerns of many countries in the Region. One session in the meeting will be a scientific debate bearing the title of “Regional perspectives on human genetics”.

In conclusion, two salient points of considerations have been brought to this meeting for the ACHR members:

1. Within the framework of general understanding of human genetics, what will be the regional perspectives on the ethical, legal and social implications of human genetics?

2. Having requested to participate in the work of the development of a Special Report on ELSI of human genetics by the Global ACHR, what and how can the Region contribute?

REFERENCE DOCUMENTS


3. WHOHQ, Work Plan for the ELSI of Genetics, a draft for discussion, Management of Non-communicable diseases, March 2001 (unpublished)

4. WHOHQ, minutes ACHR special report on genomics, Geneva, March 22, 2001, Room X10
FURTHER READINGS

Nuffield Council on Bioethics, Mental Disorders and genetics, 1998


Poste G., Bell J., Davies K., Goodfellow P. and Hastie N.; Impact of genomics on healthcare, British Medical Bulletin Vol. 55, Number 2, The Royal Society of Medicine Press Ltd. 1999


Journal of Medical Ethics, BMJ, Volume 25, Number 2, April 1999


Williamson.R., The Role of the World Health Organization in meeting the ethical challenges of the new genetics, 2001 (Unpublished)