EDITORIAL

BIOMEDICAL RESEARCH INVOLVING HUMAN SUBJECTS

Biomedical research involving humans is an emotive issue but paradoxically an essential component in an attempt to improve diagnostic, therapeutic and prophylactic procedures and promote human health. Research data obtained with laboratory animals cannot be extrapolated to predict possible effects of new drugs in humans without being validated in clinical trials. Nevertheless such data is mandatory in weeding out potentially harmful drugs. In some cases these are no suitable laboratory animal models particularly with respect to chronic toxicity such as teratogenicity, carcinogenicity and mutagenicity. Even where suitable animal models are available (for example the chimpanzee) the number of animals used in the experiment is too small to have any meaningful predictive value for a drug which will be used by millions of people.

Having accepted the necessity of biomedical research, it became necessary to put in place strict measures to safeguard and minimize possible harmful effects to the research subjects. The most important of these measures are incorporated in the "Declaration of Helsinki" adopted by the 18th World Medical Assembly meeting in Helsinki, Finland in 1964. This declaration was amended during the 29th World Medical Assembly in Tokyo, Japan in 1975, during the 35th World Medical Assembly, Venice, Italy in 1983, at the 41st World Medical Assembly in Hong Kong 1989, at the 48th General Assembly, Somerset West, South Africa in 1996 and Edinburgh, Scotland in the year 2000. The highlights of this declaration can be summarized as follows:-

(a) Biomedical research involving human subjects must conform to generally accepted scientific principles and should be based on adequately performed laboratory and animal experimentation and on a thorough knowledge of the scientific literature.

(b) The design and performance of each experimental procedure involving human subjects should be clearly formulated in an experimental protocol which should be transmitted for consideration, comment and guidance to a specially appointed committee independent of the investigator and the sponsor that this protocol is in conformity with the laws and regulations of the country in which the research experiment is performed. Biomedical research involving human subjects should be conducted only by scientifically qualified persons and under the supervision of a clinically competent medical practitioner. The responsibility for the human subject must always rest with a medically qualified person and never rest on the subject of the research, even though the subject has given his or her consent. Biomedical research involving human subjects cannot legitimately be carried out unless the importance of the objective is in proportion to the inherent risk to the subject.

(c) Every biomedical research project involving human subjects should be preceded by careful assessment of predictable risks in comparison with foreseeable benefits to the subject or to others. Concern for the interests of the subject must always prevail over the interests of science and society.

(d) The right of the research subjects to safeguard his or her integrity must always be respected. Every precaution should be taken to respect the privacy of the subject and to minimize the impact of the study on the subject's physical and mental integrity and on the personality of the subject.

(e) Researchers should abstain from engaging in research projects involving human subjects unless they are satisfied that the hazards involved are believed to be predictable. Researchers should cease any investigation if the hazards are found to outweigh the potential benefits.

(f) In publication of the results of his or her research, the researcher is obliged to preserve the accuracy of the results.

(g) In any research on human beings each potential subject must be adequately informed of the aims, methods, anticipated benefits and potential hazards of the study and the discomfort it may entail. He or she should be informed that he or she is at liberty to abstain from participation in the study and that he or she is free to withdraw his or her consent to participate at any time. The researcher should then obtain the subject's freely given informed consent, preferably in writing.

(h) When obtaining informed consent for the research project the researcher should be particularly cautious if the subject is in a dependent relationship to him or her or may consent under duress. In that case the informed consent should be obtained by a physician who is not engaged in the investigation and who is completely independent of this official relationship.

(i) In case of legal incompetence, informed consent should be obtained from the legal guardian in accordance with legislation. Where physical or mental incapacity makes it impossible to obtain informed consent, or when the subject is a minor, permission from the responsible relative replaces that of the subject in accordance with national legislation. Whenever the minor child is in fact able to give consent, the minor's consent must be obtained in addition to the consent of the minor's legal guardian.

(j) The research protocol should always contain a statement of the ethical considerations involved and should indicate that the principles enunciated in the present declaration are complied with.

Many of the drugs used to treat parasitic diseases in the tropical countries (malaria, leishmaniasis, trypanosomiasis, amoebiasis and helminthiasis) are launched prematurely without adequate data. Multinational companies are often accused of criminal negligence for introducing such drugs without adequate clinical data. It is however important to appreciate the mitigating factors which contribute to this apparent anomaly. Firstly, many multinational companies are based in Europe, North America and Japan where it is not possible to conduct clinical trials since the diseases are only endemic in tropical countries. Secondly, multinational pharmaceutical companies are not charities and are reluctant to invest vast amounts of human and financial resources in research where anticipated financial return is low. The incidence of such diseases as leishmaniasis and onchocerciasis in the tropics is low and the target population often too poor to afford expensive drugs. Thirdly, once the drugs are developed, they are subject to piracy by non-research based companies even before the innovator has recovered the cost of development which runs into millions of dollars.

A complete pharmacological profile of any drug is obtained after many years of continuous use. Indeed any time a patient is given a drug, he/she is participating in biomedical research without knowing. Even for such drugs as paracetamol and aspirin which have been in clinical use for more than 50 years, new research data is still being published. It is not uncommon for a drug which has been in continuous clinical use to be withdrawn after more than 10 years on account of new data.

Editor-in-Chief