The Role of Ethics in the Rational Use of Medicines
The Role of Ethics in the Rational Use of Medicines
“...and never do harm to anyone.”*

*Hippocratic Oath (4th Century B.C.)
# Contents

Abbreviations .............................................................................. vii  
Acknowledgements ...................................................................... ix  
Foreword ..................................................................................... xi  
1 Executive Summary ................................................................ 1  
2 Introduction ......................................................................... 10  
   2.1 Legality, morality and medical ethics ............................... 11  
   2.2 Human rights approach in rational use of medicines ................ 11  
   2.3 Unethical practices .......................................................... 14  
   2.4 Codes of medical ethics ..................................................... 17  
3 Regional Perspective ............................................................. 19  
4 Role of the Researcher ......................................................... 20  
   4.1 Drug development research ............................................ 20  
   4.2 Clinical research and clinical trials ................................... 22  
   4.3 Epidemiological, behavioural and health systems research ............... 27  
5 Ethical Obligations of the Pharmaceutical Industry .............. 29  
   5.1 Drug development ........................................................... 30  
   5.2 The pharmaceutical industry and the medical profession: providing information and advertising .................. 31  
   5.3 Interactions with other players .......................................... 32
<table>
<thead>
<tr>
<th>Section</th>
<th>Title</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>6</td>
<td>Ethical Obligations of the Medical Profession</td>
<td>36</td>
</tr>
<tr>
<td></td>
<td>6.1 Rational prescribing</td>
<td>36</td>
</tr>
<tr>
<td></td>
<td>6.2 Medical education and the continuing education programme: tools</td>
<td>39</td>
</tr>
<tr>
<td></td>
<td>for rational prescribing</td>
<td></td>
</tr>
<tr>
<td></td>
<td>6.3 Providing information to the patient and the public</td>
<td>40</td>
</tr>
<tr>
<td></td>
<td>6.4 Links with the national drug regulatory agency</td>
<td>41</td>
</tr>
<tr>
<td></td>
<td>6.5 Responsibilities of the medical profession</td>
<td>41</td>
</tr>
<tr>
<td>7</td>
<td>Role of the Government</td>
<td>43</td>
</tr>
<tr>
<td></td>
<td>7.1 Drug policy and regulation</td>
<td>43</td>
</tr>
<tr>
<td></td>
<td>7.2 Enhancing access to essential medicines and adequate drug</td>
<td>44</td>
</tr>
<tr>
<td></td>
<td>treatment</td>
<td></td>
</tr>
<tr>
<td></td>
<td>7.3 Clinical trials registry</td>
<td>48</td>
</tr>
<tr>
<td></td>
<td>7.4 Training activities</td>
<td>49</td>
</tr>
<tr>
<td>8</td>
<td>Ethics in Public Health</td>
<td>52</td>
</tr>
<tr>
<td></td>
<td>8.1 The multilateral agreement on Trade Related Aspects of Intellectual Property Rights (TRIPS)</td>
<td>52</td>
</tr>
<tr>
<td></td>
<td>8.2 Donation of medicines in emergencies</td>
<td>53</td>
</tr>
<tr>
<td></td>
<td>8.3 WHO and civil society collaboration</td>
<td>54</td>
</tr>
<tr>
<td></td>
<td>8.4 Role of the media</td>
<td>55</td>
</tr>
<tr>
<td>9</td>
<td>The Way Forward: Tackling Priority Issues</td>
<td>56</td>
</tr>
<tr>
<td></td>
<td>9.1 Identification of problem areas</td>
<td>56</td>
</tr>
<tr>
<td></td>
<td>9.2 Strategies for improving the rational use of medicines</td>
<td>56</td>
</tr>
<tr>
<td>10</td>
<td>Conclusions</td>
<td>58</td>
</tr>
<tr>
<td>11</td>
<td>References</td>
<td>59</td>
</tr>
<tr>
<td>Abbreviation</td>
<td>Description</td>
<td></td>
</tr>
<tr>
<td>--------------</td>
<td>-------------</td>
<td></td>
</tr>
<tr>
<td>AIDS</td>
<td>acquired immunodeficiency syndrome</td>
<td></td>
</tr>
<tr>
<td>CIOMS</td>
<td>Council for International Organizations of Medical Sciences</td>
<td></td>
</tr>
<tr>
<td>EDM</td>
<td>Essential Drugs and Medicines Policy</td>
<td></td>
</tr>
<tr>
<td>EPI</td>
<td>Expanded Programme on Immunization</td>
<td></td>
</tr>
<tr>
<td>ESA</td>
<td>Economic and Social Affairs (a Department of the United Nations)</td>
<td></td>
</tr>
<tr>
<td>FERCAP</td>
<td>Forum for Ethical Review Committees in Asia &amp; the Western Pacific</td>
<td></td>
</tr>
<tr>
<td>GCP</td>
<td>good clinical practice</td>
<td></td>
</tr>
<tr>
<td>HIV</td>
<td>human immunodeficiency virus</td>
<td></td>
</tr>
<tr>
<td>HPV</td>
<td>human papilloma virus</td>
<td></td>
</tr>
<tr>
<td>HSV</td>
<td>herpes virus</td>
<td></td>
</tr>
<tr>
<td>CESCER</td>
<td>Committee on Economic, Social and Cultural Rights</td>
<td></td>
</tr>
<tr>
<td>IPR</td>
<td>intellectual property rights</td>
<td></td>
</tr>
<tr>
<td>MDG</td>
<td>Millennium Development Goal</td>
<td></td>
</tr>
<tr>
<td>NGO</td>
<td>Non-governmental Organization</td>
<td></td>
</tr>
<tr>
<td>PAR</td>
<td>policy, access and rational use (of medicines)</td>
<td></td>
</tr>
<tr>
<td>RUM</td>
<td>rational use of medicines</td>
<td></td>
</tr>
<tr>
<td>SEARO</td>
<td>Regional Office for South-East Asia</td>
<td></td>
</tr>
<tr>
<td>SIDCER</td>
<td>Strategic Initiative for Developing Capacity in Ethical Review</td>
<td></td>
</tr>
<tr>
<td>TB</td>
<td>tuberculosis</td>
<td></td>
</tr>
<tr>
<td>TDR</td>
<td>Tropical Diseases Research (Research and Training in Tropical Diseases)</td>
<td></td>
</tr>
<tr>
<td>TRIPS</td>
<td>trade related aspects of intellectual property rights</td>
<td></td>
</tr>
<tr>
<td>WHA</td>
<td>World Health Assembly</td>
<td></td>
</tr>
<tr>
<td>WHO</td>
<td>World Health Organization</td>
<td></td>
</tr>
</tbody>
</table>
Acknowledgements

The support provided by Dr Samlee Plianbangchang, Regional Director, WHO South-East Asia Region in the conceptualization and development of this document is gratefully acknowledged.

WHO gratefully acknowledges contribution of those mentioned below in developing this monograph. Prof. Ranjit Roy Chaudhury, former President and Patron, Delhi Society for Promotion of Rational Use of Drugs, for preparing the first draft. Valuable inputs were made by the following individuals who, in addition to contributing to the background papers, assisted in reviewing and further developing the document: Dr K. Balasubramaniam, Adviser and Coordinator, Health Action International (Asia-Pacific), Colombo; Professor Zulfiqar A. Bhutta, Chairman, Department of Paediatrics and Child Health, The Aga Khan University Medical Centre, Karachi; Dr Vichai Chokevivat, Chairperson, Forum for Ethical Review Committees in Asia & the Western Pacific (FERCAP), and Director General, Department for Development of Thai Traditional and Alternative Medicines, Ministry of Public Health, Bangkok; Prof. Anoja Fernando, Senior Professor of Pharmacology, Faculty of Medicine, University of Ruhuna, and Chairperson, Ethical Review Committee, Sri Lanka Medical Association, Colombo; Dr Harsh Vardhan, Former Health and Education Minister, Government of National Capital Region, Delhi; Prof. Raveendra L. Jayakody, Head, Department of Pharmacology, University of Colombo; Dr Suriadi Gunawan, Member, National Commission on Ethics of Health Research and Adviser, UNAIDS Indonesia, Jakarta; Dr Harun-ar-Rashid, Director, Bangladesh Medical Research Council, Dhaka; Dr Nobhojit Roy, Head, Department of Surgery, Bhabha Atomic Research Centre Hospital, Mumbai; Dr Sri Suryawati, Director, Centre for Clinical Pharmacology and Drug Policy Studies, Gadjah Mada University, Yogyakarta; Prof. S.D. Seth, Chairperson, Forum
for Ethical Review Committee of India (FERCI) and Chair, Clinical Pharmacology, Indian Council of Medical Research, New Delhi and Dr Kathleen Holloway, Department of Medicines Policy and Standards (PSM), WHO/HQ, Geneva.

Special thanks are extended to WHO Regional Office staff: Dr Myint Htwe, Director, Programme Management; Dr Sultana Khanum, Director, Health Systems Development; Dr Krisantha Weerasuriya, Regional Adviser, Essential Drugs and other Medicines; Dr Kin Shein, Former Regional Adviser, Essential Drugs and Medicines Policy for their technical contribution and support for final production of this document.
Rational use of effective medicines can contribute immensely to better health. However, the irrational use of medicines has become a major public health problem worldwide and should not be ignored. This phenomenon is seen as; (a) using too many medicines per patient that could result in drug interactions; (b) antimicrobials often used in inadequate doses and for insufficient duration thereby causing development of drug resistant micro-organisms; (c) use of injections when oral medication is more appropriate, thereby increasing the cost of treatment; (d) medicines prescribed not according to standard treatment guidelines and prescribing policies; and (d) self-medication with prescription-only medicines.

The health care professionals and administrators as well as drug regulatory authorities, the pharmaceutical industry, drug development researchers and clinical researchers must play their respective roles in order to ensure the rational use of medicines. The increasing commercial environment in which health care operates makes this difficult, but to be oblivious to accepted codes of conduct that are based on ethics would eventually create inequity in access to health care, which is a fundamental human right. Therefore, ethical interventions should be applied effectively to reduce irrational use of medicines. This underscores the need for observing ethical principles in performing the duties and responsibilities by various groups of people who are involved in the field of medicines including the prescriber, the dispenser, the pharmaceutical company and the patient.

The prescriber must ensure that prescribed medicines are efficacious, safe and cost-effective. The prescriber must be well conversant with new medicines, their side effects and new developments in treatments. The dispenser must ensure that effective medicine of good quality is given to the right patient, in the prescribed
dose, quantity and duration, with clear instructions, and in a package that maintains the potency of the medicine. The pharmaceutical company must observe ethical criteria for medicinal drug promotion, which stresses accurate, truthful and up-to-date information. Promotion of medicines should be in conformity with acceptable ethical standards in spite of variations of such standards in different parts of the world in different societies. The patient must be compliant in taking medicines judiciously and rationally as prescribed. Ethics, therefore, has an important role to play in improving the use of medicines.

To strengthen enabling factors, there must be a comprehensive national policy on medicines with ethics as an indispensable component for promoting the rational use of medicines. Appropriate regulations should underpin the ethical principles. The infrastructure for such activities needs to be developed or strengthened, and supported by adequate financial and human resources.

There is a need to increase awareness among all relevant parties regarding the need to follow ethical principles in the use of medicines. In order to bring ethics to the forefront in improving the use of medicines, innovative measures will need to be identified, tested, applied and evaluated. Professional interest in ethics must be increased and sustained. Ethics, in fact, must constitute a core principle in making daily decisions in the medical and allied professions.

I am confident that this publication will be a beginning in creating the necessary awareness among health professionals to the vital role of ethics in the rational use of medicine.

Samlee Plianbangchang, M.D., Dr.P.H.
Regional Director
The Role of Ethics in the Rational Use of Medicines

Introduction

The Constitution of the World Health Organization states that, “The enjoyment of the highest attainable standard of health is one of the fundamental rights of every human being….” Equity and social justice are basic tenets in the delivery of health services including health care. Availability, accessibility and affordability of essential medicines are indispensable in any health service and health care system. One of the UN’s Millennium Development Goals is to “Develop a global partnership for development.” Its target No. 17 is access to affordable essential medicines in developing countries for sustaining development and in poverty elimination.

Improving access to essential medicines without improving their rational use could result in wastage of scarce resources and widespread health hazards. WHO estimates that about half of all medicines are inappropriately prescribed, dispensed or sold and that about half of all patients fail to take their medicines properly. Thus, medicines are prescribed when they are not needed; wrong, ineffective or unsafe medicines are prescribed; effective and available medicines are underused or they are not used correctly. Some of this wastage is due to unethical practices of the prescriber, dispenser and/or the manufacturer. Thus, disregarding ethics adversely affects health. Nevertheless, there is very little attention given to ethics in the rational use of medicines.

WHO is promoting ethics in the ambit of rational use of medicines since unethical practices can be present at every stage in the medicines
chain, which includes (a) research and development of new medicines; (b) clinical trials; (c) registration; (d) manufacture; (e) patents; (f) prices; (g) distribution; (h) donations, and (i) promotion of medicines.

The primary objective of this document is to emphasize ethical codes of conduct with reference to the following four categories of people – (a) the researcher who discovers and develops medicines; (b) the pharmaceutical manufacturer who produces and promotes its products; (c) the medical and allied professions who prescribe and dispense medicines; and (d) the government who regulates and controls medicines. This document also intends to create awareness of the crucial role of ethics and to advocate it in promoting the rational use of medicines. It also identifies priority issues and aims to motivate the four categories of people to find practical, realistic and innovative solutions and to implement programmes and activities that would ensure the rational use of medicines.

Regional perspective

WHO has been promoting the rational use of medicines in the context of national drug policies. Nevertheless, ethical norms need to be enforced at every step of the medicines chain particularly at the level of manufacture proliferating “me-too” medicines, inequitable pricing of pharmaceutical products, inadequate regulation and control of medicines, and lack of post-marketing surveillance to report adverse reactions of medicines so that they can be withdrawn from the market if necessary. There is often insufficient information on new medicines when marketed. The emergence of counterfeit drugs is becoming a disconcerting problem. These unethical issues could adversely affect the health of the people.

Role of the researcher

The role of the researcher in drug development and clinical research, including clinical trials, as well as research in health systems have been described.
There needs to be a proper balance between the development of drugs with high profit margins that benefit those in high-income countries and drugs with low profit margins that are needed in the developing world. Medicines with low profit margins such as those for treating tropical diseases must also be developed.

Clinical research in the development of drugs should be guided by Guidelines for Good Clinical Practice (GCP) for Trials on Pharmaceutical Products published by WHO, the International Ethical Guidelines for Biomedical Research Involving Human Subjects and the International Guidelines for Ethical Review of Epidemiological Studies published by the Council for International Organizations of Medical Sciences (CIOMS). For clinical trials on human subjects, information sheets and informed consent need to be written in simple and understandable language for the participants to understand the implications of being a part of the trial, the benefits and risks involved and their rights. Developing countries are becoming an arena for multi-centred clinical trials. Hence, the necessity for trials to be based on sound pillars of ethics, equity and transparency and conforming to the Helsinki Declaration and existing national ethical guidelines.

Research also needs to be carried out on health systems such as procurement and distribution of medicines, behavioural determinants and compliance in taking medicines, health and drug financing, and prices of medicines in order to be able to reform the national health systems to enhance access and improve the use of medicines.

**Ethical obligations of the pharmaceutical industry**

The pharmaceutical manufacturer has at least four obligations within the framework of corporate social responsibility particularly in a developing country. (a) Not to break the laws of the country; (b) to try and bring down the prices of medicines; (c) to keep aside some of the profits from sales of medicines for activities which could make a difference to access and rational use of medicines, and (d) ethical and responsible promotion.
The manufacturer should try and develop new medicines where there is a great need even though the profits may not be large. There must be thorough and comprehensive preclinical and clinical studies carried out before a new medicine is put in the market. In the event that a serious and unacceptable toxic effect is discovered in the preclinical or clinical studies, development of the medicine must be stopped in spite of investments that have already been made.

Ethics involved in manufacturing quality drugs and observing ethical criteria in medicinal drug promotion in developing countries have been emphasized. There is a need to encourage the manufacturer to provide full information on drugs under study, particularly through a system such as clinical trial registry. The pharmaceutical manufacturer should be required to observe the code of conduct regarding its relationship with the prescriber. The pharmaceutical company has the obligation to share information on the new medicine that it is marketing particularly its possible adverse effects even if it means that the use of that medicine will become limited.

The pharmaceutical industry is associated with many sectors related to the use of medicines. The pharmaceutical manufacturer must be involved in applying ethical principles in the following areas of work: clinical trials, registration, manufacturing, patents, prices, distribution, donations, promotion, utilization, prescribing, dispensing, and regulation.

**Ethical obligations of the medical profession**

The medical profession needs to play a greater role in ethical use of medicines. Doctors have responsibilities in the following six areas:

Doctors should attempt, as much as possible, to prescribe medicines within the list of essential medicines, which are prepared and regularly updated as a part of the effort to enhance access and proper use of medicines.

Modules on rational use of medicines should be included in the undergraduate curriculum of doctors, pharmacists and nurses. Experienced prescribers need to give time, experience and expertise
in the preparation of lists of essential medicines for different levels of health care, national and hospital formularies and standard treatment guidelines.

The prescriber must inform the patient about the prescribed medicines. Prescribers with experience in communications should write articles providing objective information about medicines and their rational use and publish them in the popular press and address public meetings when invited.

The medical professional must be free to publish the results of the clinical trial objectively even if they are not favourable for a new medicine that has been developed. The Drug Regulatory Agency has an ethical responsibility to regulate the pharmaceutical industry and to enforce regulation in favour of truthful and objective information.

The doctor-patient relationship based on ethics, empathy and trust, has functioned for ages. However, doubt and suspicion have emerged in some instances due to overarching commercial interests. Individually, doctors should follow the ethical codes and Medical Councils should regulate the profession to maintain and strengthen the traditional relationship. As professionals, doctors are not expected to have any other overriding considerations than providing the best professional services to their patients.

Patient empowerment by the prescriber can make the patient responsible for his or her own treatment. Basic information such as how to, when to and how long to take the treatment promote better use of medicines.

**Role of the government**

The government has a major role to play in improving the national medicines situation through proper planning and effective management. The overriding issue is that of equity for those who are underserved and those living in remote areas.

The government has ethical responsibilities in the formulation and implementation of the national medicines policy, to ensure an
effective regulatory control on quality, safety and efficacy of medicines, to enhance access to medicines, and to improve their rational use. The drug policy should lay down the tenets of rational use of medicines, base the selection of medicines on the Essential Medicines concept, and ensure their availability at reasonable cost.

Improving access to essential medicines in line with the Millennium Development Goals (Target 17) has four components: (a) rational selection and use; (b) affordable prices; (c) sustainable financing, and (d) reliable supply and health systems.

The government’s programme to improve therapeutics, reduce costs and provide an ethical framework for use of medicines needs to contain the following elements: (a) selection of lists of essential medicines for different levels of health care; (b) procurement of essential medicines by pooled procurement; (c) setting up a good quality assurance system; (d) an efficient distribution system, and (e) rational prescribing of medicines.

In May 2005, the Fifty-eighth World Health Assembly adopted a resolution WHA58.34 on the Ministerial Summit on Health Research held in Mexico in 2004. One of the recommendations of the ministerial summit was to establish the International Clinical Trial Registry Platform to set international norms and standards for clinical trial registration and reporting. The purpose of the Registry is to ensure that all clinical trials are registered and thus publicly declared and identifiable so as to ensure that for all trials, a minimum set of results will be reported and made publicly available. This will further improve research practice, assist in making treatment decisions, and help increase public trust in clinical research.

Training programmes are indispensable for procurement, storage and distribution of medicines and rational prescribing. The responsibilities and obligations of the government include encouragement to medical and related institutions to include topics on the rational use of medicines in the undergraduate curriculum. The government also needs to encourage relevant institutions and organizations to develop standard treatment guidelines, national and
hospital formularies, and guidelines for use of medicines in children and the elderly based on the National Essential Medicines List. The government should also sponsor health systems research to increase access and the rational use of medicines.

The other vital responsibilities and obligations of the government include removal of all unapproved drugs from the market, elimination of counterfeit drugs, punitive action against unjustified claims on medicines, controlling prices at an affordable level and to ensure proper labeling of medicines.

**Ethics in public health**

There is a need to ensure the application of ethics in public health. Four topics are taken up in this section and are summarized below.

The TRIPS Agreement has provisions for compulsory licensing and parallel importation, that are reiterated in the Doha Declaration, thus enabling promotion and marketing of generic medicines at affordable prices. Some bilateral and regional free trade agreements now being entered into contain TRIPS-plus provisions that limit the right to use all available flexibilities contained in the TRIPS agreement. It would be in the interest of the developing countries to negotiate Intellectual Property Rights (IPRs) at the multilateral level to safeguard what has been achieved.

Donation of medicines in emergencies brings with it many problems such as irrelevance to needs, dumping of unwanted or close-to-expiry stocks, inability to understand the language in labeling, doubtful quality of medicines, high declared value and inappropriate quantities. Core principles should be applied to improve the donation of medicines.

The family, neighbours in the community and civil society in general influence the use of medicines by an individual. To remedy the inappropriate use of medicines in civil society as a whole, there is a need for educating the public through increased coverage of the issue by the mass media and improving access to objective and understandable information.
The media can play an important role by highlighting the need for the proper use of medicines. The media should contribute in increasing awareness of the community regarding the rational use of medicines and to assist in disseminating objective, correct and concise information regarding the medicines that are available over the counter. This can promote their rational use.

**The way forward: tackling priority issues**

In future, strategies to improve rational use of medicines should be based on priority issues such as:

- regulations based on ethics, equity and transparency;
- research based on Good Clinical Practice;
- drug development based on needs of countries including orphan drugs, antimalarials and antituberculosis medicines, among others;
- marketing to be coupled with post-marketing surveillance for adverse reactions that are important for regulatory control;
- proper professional conduct observed by all stakeholders in the medicine chain: e.g. in research and development, clinical trials, registration, manufacturing, patents, prices, distribution, donations and promotion.

Ethics should form an indispensable component of the strategy in promoting the rational use of medicines.

**Conclusions**

The rational use of medicines has a strong component of ethics and equity. People have a right to medicines and access to good quality medicines must be ensured. They must also be used rationally. In this regard, there are ethical responsibilities of (a) the researchers in their quest for new medicines, (b) pharmaceutical manufacturers in their production and promotion of medicines, (c) members of the medical and allied professions in their prescribing, and dispensing of medicines.
and (d) the government in developing national medicines policy that will ensure access to essential medicines and their rational use, among others. If the four groups work diligently within the framework of ethics and equity, the situation with regard to rational use of medicines is sure to improve. It is with this hope that this document on the Role of Ethics in the Rational Use of Medicines has been published.
One of the Principles of the Constitution of the World Health Organization states – “The enjoyment of the highest attainable standard of health is one of the fundamental rights of every human being without distinction of race, religion, political belief, economic or social condition.” Access to essential medicines and their rational use are crucial elements in the delivery of health care and can be seen as a part of the fundamental right to health.

Equity and social justice are basic tenets in the delivery of health services in general and health care in particular. Availability, accessibility and affordability of essential medicines are indispensable in any health service. Even so, more than 50% of medicines are prescribed, dispensed, or sold inappropriately and about 50% of patients do not take them correctly throughout the world (1, 2). Thus, medicines are prescribed when they are not needed; wrong, ineffective or unsafe medicines are prescribed; effective and available medicines are underused or they are not used correctly. Some of this wastage is due to the unethical behaviour of the prescriber, the dispenser or the drug manufacturer. Thus, disregarding ethics adversely affect health. Ethics, therefore, needs to have a better focus in the rational use of medicines within the strategic framework of ethics in health. Ethical approaches should complement and be in concert with other approaches and interventions in promoting the rational use of medicines.

Often, the interactions involving medicines take place beyond the spotlight of regulation. When doctors prescribe for patients and medical representatives meet doctors or pharmacists who dispense
medicines, there is no supervision. Hence, there is need for ethics in guiding the doctor, the medical representative and the pharmacist in these encounters. Without ethics, these meetings become mere commercial transactions. Ethics translates and elevates it into an activity that is guided by considerations of equity and fairness.

2.1 Legality, morality and medical ethics

The application of ethical principles is essential in selecting and justifying actions and policies designed to protect people’s rights, maximize their welfare, and avoid harm. Medical ethics is the application of ethical principles and ethical reasoning in medical decision-making. Key concepts in medical ethics include confidentiality, consent, fairness or equity, harm and benefit, honesty and self-determination (thinking, choosing, deciding and acting for oneself).

Problems that are encountered in the field of medicine often involve ethics as well as law. These two entities have a reciprocal relationship and are mutually inclusive – what is ethical or moral is also legal. The law provides the framework by which ethical choices or decisions that are made can be seen to be within the limits of the law. Consideration of legality is done with reflection of ethical or moral values that are accepted by the profession. Therefore, legality, morality and ethics are basic tenets that should be taken into consideration in realizing the fundamental right to health which includes availability, accessibility and affordability of medicines.

2.2 Human rights approach in rational use of medicines

The last 20 years has witnessed an upsurge of interest and activities in the field of rational use of medicines. The World Health Organization (WHO) took the lead after the international conference on Primary Health Care held in Alma Ata in 1978 and identified “Provision of essential drugs...” as one of the eight components of primary health care (3). Although strategies for providing access to medicines have been implemented as well as components of such strategies (for example, lists of essential medicines, quality assurance, pooled
procurement, rational prescribing and enhanced compliance) the ethical aspects of rational use of medicines appear to have been overlooked. WHO and other organizations are now increasingly supporting rational use of medicines programmes and activities collectively or independently. This has been reiterated in the document, “WHO Medicines Strategy 2004-2007” (2). The use of unnecessary medicines leads to wastage of resources at the individual, family and national levels. This wastage is compounded by the fact that about 33% of the world’s population have no regular access to medicines. It is quite clear that the UN Millennium Development Goals (4) will not be achieved unless the situation regarding access to medicines improves. This has been recognized in the Task Force paper written for the United Nations Millennium Summit on HIV/AIDS and Access to Essential Medicines. Access to medicines can be improved by improving rational use through decreasing unnecessary and inappropriate use as well as wastage.

One would have expected much more emphasis to be placed on ethical considerations with regard to the rational use of medicines. The Task Force paper, for example, has dealt with overarching barriers under the following headings: human right to health, role of gender and women’s status, economic dimensions, cultural dimensions and traditional medicines. However, the human right to health does not mention rational use of medicines at all other than mentioning in passing that in May 2000, the Committee on Economic, Social and Cultural Rights (CESCR) specifically elaborated its Article 12 to include the right to essential medicines. The Millennium Development Goal cites access to affordable essential medicines in developing countries (target No. 17) for sustaining development and poverty elimination.

The World Health Organization has taken steps to bring ethics into the ambit of rational use of medicines. In the WHO Medicines Strategy 2004-2007 (2), it is clearly stated that over the next four years WHO “will advocate a rights-based approach as one additional means to promote access to essential medicines”. In the same section, the WHO Medicines Strategy states that many examples of corruption and lack of ethical practices in the pharmaceutical arena are reported
in the press and scientific journals. Unethical practices are present at every stage in the drug or medicines chain. The various elements of the chain are:

- research and development of new drugs;
- clinical trials;
- registration of new medicines;
- manufacturing;
- patents;
- prices of medicines;
- distribution of medicines;
- donations of medicines;
- promotion of medicines.

It is important at the outset to discuss the human rights approach to health care and look at the framework of this approach. The Universal Declaration of Human Rights (1948) affirms that “everyone has a right to a standard of living adequate for his and his family’s health”. The International Covenant on Economic, Social and Cultural Rights recognizes “the right of everyone to the highest attainable standard of physical and mental health”. The Task Force Paper states that by 2001, 193 countries had recognized the right to health in their law or constitution.

The link between ethics and the rational use of medicines was recently highlighted by Dr Samlee Plianbangchang, Regional Director of the South-East Asia Region of the World Health Organization when he delivered a keynote address on “Equity and responsibilities in providing access to medicines: the roles of physicians, researchers, manufacturers and governments” at the International Conference on Health Research and Access to Medicines in Asia and the Western Pacific. The meeting was organized by the Forum for Ethical Review Committees in Asia and the Western Pacific (FERCAP) at Chiang Mai, Thailand in December 2004 (5). For the first time, the speaker delineated the responsibilities of the different stakeholders in following ethical principles in the use of medicines.
It is hoped that in future, more emphasis will be laid on ethical practices relating to different aspects of the medicines chain and that strategies will be formulated and implemented to root out unethical practices that lead to inequity, injustice, and adversely affect health, particularly of the poor and the marginalized.

2.3 Unethical practices

Any unethical, illegal and unjustified action at any of the links which form the medicines chain will adversely affect the consumer. It is therefore important to mention a few of the malpractices that have occurred in the last two decades in order to think of ways of combating this hazard. The remaining part of this document will deal with ways in which the four different players could help in promoting ethical considerations and values in the production, distribution, sale and use of medicines. It is neither possible nor relevant to list all the unethical practices that are prevalent. Just a few will be mentioned under the following headings.

Unauthorized clinical trials

This is one area where there is a need to regulate the unethical and unauthorized clinical trials being carried out particularly in the developing countries where the regulatory systems need strengthening. These unethical practices will grow unless strong action is taken because the pharmaceutical manufacturer and the clinical research organization want to conduct clinical trials in their own interests. There is an abundance of clinical material available in developing countries in contrast to the developed countries. There is a population that has probably not been exposed to medicines which are good material for clinical trials. There are well-qualified clinicians in these countries who would be available and would be glad to take part in multicentre clinical trials. Finally, the cost of carrying out clinical trials in a developing country would be a fraction of the cost in the United States of America, United Kingdom or Europe, even if the numbers needed were available. An associated factor is the weak drug regulatory system in developing countries.
All these factors make it possible for unethical clinical trials to be undertaken. Sometimes the trials are carried out without approval from the national drug regulatory agency. There have been instances where the national government has ordered the withdrawal of a drug from a clinical trial or from the market and yet the drug continues to circulate in the country and even clinical trials are conducted. In some instances, there is an unethical collusion between the pharmaceutical company and the doctor. The clinician may be given inducements in addition to a legitimate fee for every patient recruited. Such inducements could be travel for the clinician and his family to a famous city or country for a medical conference, or could even be monetary, or material in nature. These instances occur not only in developing countries but also in developed countries.

Ownership of the data emanating from clinical trials is an issue that needs to be discussed. Does this belong to the pharmaceutical sponsor of the trial or to the investigator who carried out the trial or does it belong to the institute or medical centre that allows the clinical trial to be undertaken? Sometimes, side effects noted are not publicized and more often than not, if the new drug is not found to be as effective as expected, the results are not published. The WHO Medicines Strategy 2004-2007 states that “there is real conflict of interest between manufacturers and researchers. Good clinical practices are not always respected in poorer countries and adverse findings are not published or falsified”. Clinical trials therefore definitely pose an ethical challenge at present and in the future.

**Unethical advertising**

Another visible unethical practice which needs to be curbed is unjustified advertising of a company’s products. The public is exposed to advertising by pharmaceutical companies either on the radio or on television and incorrect statements are made to persuade doctors and patients to prescribe or use a particular medicine. In many developing countries any person can go to a pharmacy or dispensary and ask for a particular medicine – even an antibiotic – without a prescription. Direct advertising to consumers without regulation could lead to irrational use and unnecessary expenditure. This practice of
advertising unjustified claims takes on a new dimension when herbal
drugs are openly advertised as a cure for serious diseases such as
arthritis, epilepsy and cancer. The public needs to be protected from
this unethical and unjustified high-pressure salesmanship. The
pharmaceutical industry should follow the Ethical Criteria for Medicinal
Drug Promotion as enunciated in the document brought out by WHO
in 1988 (6).

**Counterfeit medicines**

Manufacture of counterfeit medicines or medicines without any or
deliberately reduced active ingredients is another reprehensible
unethical practice that can harm the patient. It is unethical for any
government to allow this to continue.

There are many other unethical practices that take place all the
time. Some of these will be dealt with later under measures that need
to be taken to curb unethical practices. These include bribery at the
level of registration of new medicines, pricing of medicines and erratic
and inefficient procurement and distribution.

This document will deal with the four major players in the
medicines chain who are capable of ensuring that ethical practices
are followed. If this could be done, nearly all persons, and definitely
those below the poverty line would be able to receive a range of
about 20 medicines of good quality. These medicines would take
care of 85% of the common ailments. The Commission on
Macroeconomics and Health set up by the Government of India has
shown that adequate funds for enabling this are even now being spent
by the government. This money is however, not spent within a
framework of rational use of medicines and much of it is wastefully
spent. The four players in the medicines chain are:

- researchers who try to discover better and more effective
  medicines;
- pharmaceutical companies that develop, manufacture and
  market medicines;
• physicians and other health professionals who prescribe the medicines;
• the government who is responsible for regulation of medicines including quality assurance and their rational use.

These four players will be considered separately in the order following the natural history of discovery, manufacture and use of medicines (Sections 4 to 7).

2.4 Codes of medical ethics

There are three well-known codes of medical ethics. They are – the Hippocratic Oath (4th Century B.C.), the International Code of Medical Ethics (1949) and the Declaration of Helsinki (first published in 1964, the latest version printed in 2004) of the World Medical Association. The first two documents are important instruments in defining the duties of the medical doctor with respect to personal conduct in the society and in the delivery of health care. The Declaration of Helsinki provides ethical principles in medical research and sets the stage for the ethical conduct of research involving human subjects. Collectively, they form the basis for improving and promoting ethical practices in the areas of health.

This document covers a variety of ethical approaches for four groups of people; namely, the researcher, the pharmaceutical industry, the medical profession and finally the government, where ethics could play an important role in improving access, promoting equity and in ensuring the rational use of medicines. Different areas where ethics need to be emphasized such as drug development, clinical trials, provision of information, regulation and control of medicines, etc. are relevant to the four groups. Possible interventions or activities that are needed in mainstreaming ethics have been described. Hence, there is some repetition as there are common areas that need to be emphasized in each of the four groups.

Thus, the primary objective of this document is to serve as a reminder on human rights and ethical codes of conduct relevant to
the following four categories of people: (a) The researcher who is concerned with the development and discovery of drugs; (b) the pharmaceutical manufacturer who is involved in the development, production and promotion of its products; (c) the medical, pharmacy, nursing and other allied professionals who are prescribing and dispensing medicines and (d) the government who is responsible for national medicines policy development and implementation including the regulatory control of medicines. This document also intends to create awareness on the crucial role of ethics and to place stronger emphasis in this neglected area in promoting the rational use of medicines. It also identifies priority issues and aims to motivate the four categories of people to find practical, realistic and innovative solutions and to implement programmes and activities that would ensure the rational use of medicines.
The World Health Organization has been promoting the rational use of medicines within the framework of national drug policies. Ethical issues in the area of rational use have not received much emphasis. A stimulus for focusing on ethics came with reports of clinical trials that are being carried out without regulatory and ethical sanctions, flouting norms of good clinical practice. The pharmaceutical manufacturer is driven by commercial motives, proliferating “me-too” drugs and lifestyle medicines. The ethical interactions between the industry and the pricing authorities, patents, drug control, and the prescriber need to be strengthened effectively. Drug legislation and regulations exist but their effectiveness is questioned since they are unable to enforce compulsory monitoring and reporting of adverse reactions of new medicines for withdrawal from the market if necessary. The policy makers may be apathetic towards ensuring good quality of medicines and vaccines and in preventing counterfeit products from being sold. All these unethical practices endanger the health of the people. The last two decades have seen a phenomenal growth in the drug industry that is designed to recover expenses for research and development and commercial gains. Therefore, ethical norms need to be enforced at every step of the medicines chain (Section 5.3).
Drug development research is indispensable for restoring and promoting health and in contributing to overall health development. Many developing countries have made substantial investments in building and enhancing their capabilities in drug and vaccine research. Some of these efforts have been made in developed countries.

4.1 Drug development research

The scientist who is involved in research for new medicines may not be in a position to make decisions or to participate in discussions where the areas of research are decided. If, however, by virtue of his/her seniority or experience and if he/she is in a position to take such decisions, then he/she should encourage research to discover medicines for diseases prevalent in developing countries such as tuberculosis, malaria, diarrhoeal diseases and kala-azar. In fact, there have been some excellent examples in the past. Merck, in collaboration with the World Health Organization discovered the effective use of ivermectin in human onchocerciasis (river blindness) that was endemic in Africa. Unless scientists carry out research in these areas, there will never be any new medicines for these conditions. Very limited research, for example, is being carried out to discover a new medicine for tuberculosis – the last new drug having been discovered in 1963. The profits from selling these medicines will be negligible compared to the profits from medicines for cardiovascular diseases, obesity, cancer and diseases induced by stress. However, it is neither ethical nor equitable to carry out research only in those areas where huge profits are to be
made. Researchers could play a part in nudging their non-scientific colleagues to occasionally take a decision to look for medicines for diseases of the third world. There are, in fact, several policy makers and health planners who go beyond what has been written above, and who believe in ensuring research geared towards medicines for diseases widely prevalent in the developing world.

As would be expected, pharmaceutical companies and researchers in drug discovery centres in developing countries follow the same pattern. What is more interesting is that government supported research institutions also have the same philosophy of trying to discover medicines for conditions like cardiovascular disease – even though the need is for research for diseases specific to developing countries. Finally, research in traditional medicine and medicinal plants in countries with a heritage of the traditional systems of medicine is also directed towards the ailments of the developed countries and not towards finding a simple herbal preparation, for example, for diarrhoea and anaemia.

The laboratory researcher working in the field of drug development has another ethical obligation. He/she should meticulously report any toxic or undesirable effect of the compounds being evaluated in preclinical toxicology research. Very often, such a finding by the researcher may result in heavy losses for the company that has invested in that compound. It may be easier to dismiss an occasional unusual finding. This will not be ethical. In later clinical trials or in post-marketing surveillance studies, this compound may induce severe adverse effects leading even to death. The United Nations has published a Consolidated List of Products Whose Consumption and/or Sale Have Been Banned, Withdrawn, Severely Restricted or Not Approved by Governments (7). It is a long list of approximately 1100 products of which 501 products are pharmaceuticals (the rest are agricultural and industrial chemicals) as well as consumer products on which regulatory actions have been taken by 112 Governments due to their adverse effects.
4.2 Clinical research and clinical trials

An effective system of review of the ethical component of research is a crucial safeguard for participants in drug research. Developing countries should establish an effective system for the ethical review of research, which includes the establishment and maintenance of research ethics committees that are independent of government and sponsors of research. Research should be subjected to ethical review in both the country hosting and the country sponsoring the research. International initiatives should be taken for establishing research ethics committees, training their members and monitoring their development. Funding should be provided for these purposes by those who sponsor research in developing countries. Furthermore, the national and international sponsors of research should ensure that professionals involved in health research are adequately trained in the ethics of research.

The pharmaceutical companies are looking towards countries in the South-East Asia Region as potential centres for clinical trials of their products. The reasons for this have been elaborated earlier in this document (Section 2.3). Participation in international multicentre clinical trials by clinical researchers is acceptable but such a trial should be based on the sound pillars of ethics, equity and transparency. When undertaking the clinical trial of a new drug, the researcher has to keep meticulous records and report to the national drug regulatory agency and the pharmaceutical company any adverse effects observed in the use of the drug. This applies not only for Phase II and Phase III clinical trials but also to the adverse effects seen during the post marketing surveillance of a new medicine. This is an area where doctors are liable to overlook and not report what has been observed. This may lead to disastrous health consequences.

Another issue of concern to the clinical researcher is regarding the data obtained as a result of the clinical trial carried out. The data of the trial belongs to the investigator who should be free to publish the results obtained. Any constraint on this right to publish the results,
which sometimes happens if the new drug is ineffective or induces unexpected side effects, would be regarded as unethical conduct by the pharmaceutical company if it insists that no publication should be made. Withholding such information from the public domain may result in harmful effects in others that could have been avoided if the publication of the results had been made earlier.

It is the responsibility of the investigator to ensure that the clinical trial is carried out in an ethical manner conforming to the Helsinki Declaration and national ethical guidelines. Even though several persons are involved in planning and conducting a clinical trial, it is the Principal Investigator in the centre who is responsible for the ethical conduct of the trial. If things go wrong, he/she would be held responsible.

One important aspect, which is of great concern today, is the issue of informed consent. The issue of “Informed Consent” is one where ethical norms are sometimes ignored. Informed consent is participation in a medical experiment by a subject after achieving an understanding of what is involved. Recently, the newspapers highlighted a clinical trial carried out in a developed country on foster children without informed consent of the parents or the subjects (8).

**Summary of arguments about genuine consent**

In circumstances where consent to research is required, genuine consent to participate in research must be obtained from each participant. In some cultural situations, it may be appropriate to obtain agreement from the community or consent from a senior family member before a prospective participant is approached. If a prospective participant does not wish to take part in research, this must be respected. Researchers must not enroll such individuals and have a duty to exclude them from participation.

The researcher cannot carry out any clinical trial of a new drug or a procedure without obtaining informed consent of the patient or the volunteers. Many of the forms used today for obtaining informed consent are inappropriate. They are too long and cumbersome and
The Role of Ethics in the Rational Use of Medicines

provide the subject with a mass of information which he/she cannot comprehend. There is also considerable variation in the manner in which the patient is informed about the new medicine.

One of the ethical challenges in the future for the clinical researcher is to develop more appropriate and meaningful informed consent forms. One of the tenets of acceptable clinical trial protocol is that the patient or the subject in a clinical trial should benefit in some way from the clinical trial research being carried out. The researcher should try and ensure that this concept, as far as possible, is translated into actual practice when planning and conducting clinical research. One example could be that the patients who enroll in the clinical trial

Box 1: Summary of arguments about genuine consent

The principle of respect for persons requires that we do not conduct research without their consent

BUT

Sensitivity to other cultures requires that researchers pay attention to the context in which research is conducted, including customs and traditions

NONETHELESS

Sensitivity to other cultures cannot override the central requirement of respect for persons, which requires that we refrain from conducting research without consent. This is a fundamental principle, which is important to promote so as to empower vulnerable populations

THEREFORE

Genuine consent to research must be sought from all participants in research

AND

There is also a duty to develop or implement innovative practices with regard to providing clear and unbiased information and to ensure that consent to research is freely given.

Source: The ethics of research related to healthcare in developing countries (9).
are provided the medicine, free of cost, until it is available in the market. This has been clearly enunciated in the International Ethical Guidelines for Biomedical Research Involving Human Subjects (10). It says “After the clinical trial is over, if need be, it should be made mandatory that the sponsoring agency should provide the drug to the patient till it is marketed in the country”. In addition, if the trial shows the investigational drug to be better, the placebo group should be offered the drug after the trial, until it is marketed.

**Clinical trials: drug trials**

The manufacturers have certain responsibilities and obligations when initiating clinical trials with a new drug. No clinical trial should be sponsored by the pharmaceutical manufacturer without obtaining the approval of the national drug regulatory agency of the country and that of the Ethics Review Committee of the centre or institute or hospital where the trial is to be carried out. There can be no exception to this rule. All clinical trials should follow the Guidelines from Good Clinical Practice (GCP) for Trials on Pharmaceutical Products (11). Meticulous records of each of the patients on the new drug being evaluated have to be kept by the pharmaceutical company. Whenever there is danger to the life of a patient, and the code of the drug in a double blind study needs to be broken in the interest of the patient’s safety, this should be done. A proper system for monitoring the side effects seen with the new drug should be set up and all such adverse drug reactions reported to the national drug regulatory agency. These adverse reactions should be carefully recorded even when the drug has been released and particularly in the post marketing surveillance studies. If serious side effects are seen, even after release and even if it is earning the company millions of dollars, the drug should be withdrawn from the market the moment the balance between possible benefit against possible risk indicates that the risk is unacceptable.

**Clinical trials: vaccine trials**

Some of the ethical issues in vaccine research are common to all kinds of health research. However, there are certain issues that are unique in vaccine research; e.g. immunization is a convenient measure
with a track record of many spectacular successes, yet there remains a heavy burden of uncontrolled infectious diseases in countries of South-East Asia and in other developing countries of the world. Vaccination may be considered as an important approach in preventing infectious diseases in addition to treatment with medicines.

**Ethical imperative in vaccine research**

Infections continue to account for the majority of the deaths in children and adults in developing countries, for absence from work and school, and contribute to impaired growth in children. The HIV epidemic has promoted a resurgence of opportunistic infections in adults and also in children. The success of vaccination programmes, in general, has been attributable to long-term efficacy and operational feasibility. The availability of infrastructure for the delivery of vaccines in the Expanded Programme on Immunization (EPI) provides a ready-made pathway for the distribution of new vaccines if these can be demonstrated to be effective. Equity in health provision and delivery is an important ethical concern; vaccines have a greater potential for equitable distribution than many other health interventions. In view of the importance of infections and the potential benefit of vaccines, there is a strong ethical imperative to conduct vaccine research.

**Box 2: Ethical Imperative in Vaccine Research**

In order to respond more effectively and quickly to the enormous disease burden among children in developing countries, greater efforts should be made to conduct vaccine trials among such children. This would facilitate the introduction of effective vaccines to the populations with a high disease burden such as Dengue Haemorrhagic Fever. Such trials must be based on sound science and be conducted ethically.

**Participation of adolescents in vaccine trials**

The participation of adolescents in vaccine trials would be justified where adolescents may be the target population for vaccines against diseases acquired during or after adolescence, e.g. vaccines for HIV,
human papilloma virus (HPV), herpes virus (HSV) or other sexually transmitted infections. If there is some evidence of incomplete efficacy in adolescents (as compared to adults), further studies in adolescents would be indicated.

**Availability of the vaccine after the trial**

An important issue is the access of the community and/or the country that hosted the trial to the vaccine after the completion of the trial. The aim is to ensure that those participating communities and countries benefit from hosting a trial and have first call on the interventions that result from the trial. Equitable availability of vaccines after authorization for marketing of the vaccine is a desirable outcome.

In order to ensure proper protection of research participants and the highest quality of health research, ethical review systems should be established at the national, regional and/or institutional levels as appropriate. Where the system exists, it may be strengthened based on Operational Guidelines for Ethics Committees that Review Biomedical Research published by WHO (12). The International Ethical Guidelines for Biomedical Research Involving Human Subjects, and the International Guidelines for Ethical Review of Epidemiological Studies published by the Council for International Organizations of Medical Sciences (CIOMS) are useful references in establishing or strengthening ethical review committees.

**4.3 Epidemiological, behavioural and health systems research**

If access to medicines is to improve and if medicines are to be used well, which are two ethical prerogatives, then research needs to be carried out in areas that would help increase access and promote rational use. Research needs to be carried out on drug prices as it is not ethical to allow a system where one person pays a much higher price for the same medicine in the same country. The traditional areas of research have brought up some good answers but will not go further in helping to resolve some of the ethical issues.
Research needs to be carried out on health systems, on procurement and distribution of medicines, on the behavioural aspects of people taking medicines, on attempts to enhance compliance, on health financing, drug pricing and other relevant areas. The results of studies in these areas could lead to modification of national health systems leading to enhanced access to medicines. The researcher has an important role in trying to get such studies underway. This type of research needs different types of researchers who are very often not interested in carrying out research in the field of health. Economists, management specialists and social anthropologists are needed for this type of research. Also needed are experts in health systems research and in materials management to see that medicines reach every health outpost in the country, that these medicines are of good quality at the time they are taken and that the prices of these medicines are not unjustifiably high. This, however, is not always possible. The government must ensure that operational research leads to availability of medicines across the country. However, it appears to be unethical if researchers paid by government funds utilize government resources and national infrastructure to only carry out research that would advance their careers and lead to scientific recognition in a narrow field that has no relevance to the needs of the people in the country, particularly the poor. That would amount to apathy, bordering on unethical conduct.
Pharmaceutical manufacturers need to follow certain regulatory practices laid down by the laws of the country. Breaking these laws would amount not only to unethical conduct but illegal action. Then there are certain ethical obligations the pharmaceutical manufacturers have, especially within the framework of corporate social responsibility – more so when working in a developing country. There are several areas where pharmaceutical companies could make a difference in enhancing access to medicines or in improving the rational use of medicines.

Pharmaceutical manufactures have at least four ethical obligations which are:

- not to break the laws of the country;
- to try and bring down the prices of medicines;
- to keep aside some of the profits from sales of the drug for activities which could make a difference in improving access to medicines;
- ethical and responsible promotion.

Examples are given for each of these obligations.

The use of quinacrine for tubal sterilization was stopped by the national regulatory authority. Yet, it continued to be used for this purpose. Kumar reported the incident in The Lancet (13) and is an example of breaking the law of the country.

An example of bringing down the price of medicines is the dramatic fall in prices of antiretroviral drugs (14). In mid-2000 the
cost of triple combination of antiretroviral drugs produced by pharmaceutical companies in the developed world was over USD 10,000. Brazilian companies offered them at about USD 2800 in that year and Indian companies offered them in 2001 at USD 350. By 2003 prices had dropped even further and the price range was from USD 200-800. In 2006 they were available at USD 132 and the maximum was USD 560. Thus pressure from consumers, socially responsible companies and competition brought about a welcome decrease in price (thereby improving access) to a vital treatment.

Making a difference in improving access to medicines can be taken as the third example when a pharmaceutical company keeps aside a certain proportion of the advertising budget to develop drugs for mainly the poor in the third world countries where the profits would be minimal.

The last example of ethical and responsible promotion, e.g. to the medical profession, is when an advertisement of a medicine contains the name(s) of the active ingredients in approved generic name(s); indication(s) for use; precautions, contraindications and warnings and the name and address of the manufacturer or distributor.

5.1 Drug development

Manufacturers should have a social conscience and try and develop new medicines where there is a great need even though the profits may not be large. Some proportion of their enormous budget, much of it spent on advertising, should be kept aside for this type of activity. Sometimes the pharmaceutical company could provide its expertise in drug development, which could, in fact, be paid for by the national and international community. They could, as has also been done earlier, carry out preclinical toxicology studies on interesting compounds developed by others and be compensated for this work from resources, such as government funds, made available for such studies. Otherwise, these essential studies in the drug development chain would not be possible. Manufacturers should also be careful not to put new drugs on the market unless all the necessary preclinical
toxicology studies have been carried out. Several countries have not developed strong national drug regulatory agencies to critically review new drug submissions by pharmaceutical companies. The manufacturers should not take advantage of this situation. Similarly, it goes without saying that, even if millions of dollars have been spent on developing a new drug, such development should stop the moment any serious, unacceptable toxic effect is discovered.

5.2 The pharmaceutical industry and the medical profession: providing information and advertising

The pharmaceutical company has the information about the new medicine that it is marketing. This information needs to be disseminated and shared with others whenever the medicine is marketed. The pharmaceutical company must provide appropriate, correct and timely information to the medical profession for every medicine being introduced in the market. Sometimes, it has been observed that the information regarding possible side effects of a new medicine is given in detail to the physicians in developed countries while the physicians in the developing countries are given very scanty information. The same discrepancy has been seen in the package inserts providing information to the patient. e.g., most of the oral dosage forms are available in strips and thus no information is available to the patient. This is not ethical. It needs to be repeated once more, that the pharmaceutical company should not hide any information about adverse reactions of a drug, obtained from clinical trials. Such information should be immediately disseminated to the medical profession even if it limits the use of that drug. It is again not appropriate for the manufacturer of a drug to promote its use for a condition for which it has not been approved for use by the national drug regulatory authority. Countries do allow such use at the discretion of the physician but the manufacturer should not advertise or promote usage which is not approved by the drug regulatory authority. The proper ethical course would be for the pharmaceutical company to obtain approval from the appropriate authority for such use of their medicine.
5.3 Interactions with other players

Since the pharmaceutical company necessarily interacts with a large number of different players, its relationship should be ethical. The pharmaceutical companies should follow the Code of Conduct governing the relationship between members of the medical profession and the pharmaceutical manufacturers. Improper incentives should not be provided to clinical investigators to carry out clinical trials of their drugs. Improper incentives should also not be provided to practicing physicians to prescribe their products when not justified. The manufacturer needs to follow a high code of ethics in relationships with doctors. In no way should monetary incentives be provided to doctors to use their products or to drug regulatory agencies to approve use of their medicines or to members of hospitals and institutes, Drugs and Therapeutics Committees or committees for selection of medicines to put their product on the list to be purchased. Pharmaceutical companies need to inform doctors about their products. However, advertising of a product should follow ethical guidelines and not mislead the doctors or the public in the case of over-the-counter medicines. Unjustified claims about the properties of their medicine, not supported by evidence, should not be made in either the print or the electronic media. Regulation of unjustified claims to protect the public is weak in many countries. The pharmaceutical company should not take advantage of this weakness – that would be immoral and unethical. The pharmaceutical company should try and prevent pharmacies or drug stores from selling their medicines without a prescription when the country’s regulations have made it clear that a prescription from a doctor is a prerequisite for purchasing that medicine. It is realized that following many of the ethical principles may jeopardize commercial gains being made by the company. However, if the goal is to increase access and improve the use of medicines, then they have to be brought within a framework of ethics and equity.

Countries in this region have problems with substandard and counterfeit drugs circulating in the market (15). If the pharmaceutical company detects that its own medicine in circulation is sub-standard, then it should immediately withdraw from the market all batches of that medicine and inform the drug regulatory agency. If the
pharmaceutical company finds that counterfeit drugs – drugs that copy the company’s drugs – are in the market, then it should immediately inform the regulatory authority. The first reaction when a company detects such a drug being sold is to find out the source of the drug and to stop its manufacture. The company should also inform the police so that joint action can be taken.

Finally, pharmaceutical companies should support governmental and nongovernmental agencies to hold workshops on rational use of medicines and on rational prescribing. They should also sponsor workshops on the ethics of drug use and generally help in raising the quality of clinical trials and clinical research in the countries of the Region. Since medicines are critical for public health, manufacturers should always follow ethical guidelines, subordinating their benefits to the good of the public. In case such a conflict arises – e.g. if a side effect of a widely selling medicine is observed, information about this side effect should be widely disseminated, even though it will mean a fall in sales of that medicine and loss of profit to the manufacturer.

It would be interesting to look back, before completing this section, at the challenges described in the report – WHO Medicines Box 3: Responsibilities of the pharmaceutical manufacturers in ensuring access to medicines

- Responsibilities of pharmaceutical manufacturers should not only be limited to areas of drug development, production and marketing; but also in disseminating correct information about the medicines.
- The industry should work closely with other relevant players to ensure accessibility to medicines.
- The manufacturers should be socially conscious, and try to develop new drugs where there is a great need, even though the profits may not be large.
- The industry should provide adequate, correct and timely information to the medical profession on every drug being introduced in the market.

Source: Planhchangchong S. (Regional Director, WHO/SEARO). Equity and responsibilities in providing access to medicines: the roles of physicians, researchers, manufacturers and governments (5).
Strategy 2004-2007: countries at the core (2). Of the challenges covering therapeutically sound and cost-effective use of medicines by health professionals and consumers – all have an ethical component and implications, and the pharmaceutical manufacturers are closely connected with all. This is very relevant and shows how closely the pharmaceutical industry is associated with the ethical considerations in the production, quality, distribution and use of medicines.

Unethical practices could occur in each of the following areas of challenges.

- **Research and Development**
  - Most resources spent on “lifestyle” conditions and “me-too” medicines

- **Clinical Trials**
  - Real conflict of interest between companies and researchers
  - Good clinical practices not always respected in the poorer countries
  - Adverse findings not published or falsified

- **Registration**
  - Falsification of safety data
  - Bribery
  - Fast-track registration

- **Manufacturing**
  - Counterfeiting
  - Medicines for ‘orphan’ diseases
  - Tax evasion and fiscal fraud

- **Patents**
  - Excessive extension on “best-selling” medicines
  - Unlawful appropriation of royalties

- **Prices**
  - Vary between countries
  - Artificially inflated in some cases

- **Distribution**
  - Mismanagement of goals
  - Bribery

- **Donations**
  - WHO Guidelines not always respected
The Role of Ethics in the Rational Use of Medicines

- **Promotion**
  - Direct-to-consumer advertising
  - Real conflict of interest between physicians and manufacturers
  - Subtle pressure on physicians

- **Utilization**
  - Use of too many medicines (polypharmacy)
  - Inappropriate use of antimicrobials
  - Over-use of injections
  - Inappropriate self-medication
  - Non-compliance to dosing regimes

- **Prescribing**
  - Failure to prescribe according to clinical guidelines
  - Prescribing without limitation to level of expertise
  - Prescribing not according to needed quantity and duration of treatment
  - Prescribing without explaining about the medication

- **Dispensing**
  - Dispensing without clear instructions and labeling
  - Dispensing without appropriate container/packaging
  - Dispensing without keeping proper records
  - Dispensing by untrained and unlicensed individuals

- **Regulation**
  - Unsafe and non-efficacious medicines are registered and no review to de-register them
  - Availability of prescription medicines without prescription
  - Unlicensed medicine retail shops
  - No regulation on advertising and promotion
  - Availability of substandard and counterfeit drugs in the market.
6
Ethical Obligations of the Medical Profession

The last-but-one link in the medicines chain is prescribing of medicines where the medical profession has the largest role to play in the ethical use of medicines. Doctors need to help in the incorporation of concepts such as equitable access to medicines into the existing framework of governance, since each programme has its own system for selection, procurement, distribution and use of medicines, be it malaria, HIV/AIDS, TB or other diseases. The five different areas where doctors have an important role and responsibility are:

- rational prescribing;
- education and providing information to the patient and the public;
- maintaining links with the medicines regulatory authority;
- links with the pharmaceutical industry;
- helping to prepare modules and tools, e.g. standard treatment guidelines for rational prescribing.

All these, in one way or another, will help in enhancing access to medicines and their rational use.

6.1 Rational prescribing

Prescribers wherever possible, should prescribe medicines appearing in the national lists of essential medicines based on WHO’s list and those prepared by states and hospitals as part of the effort of WHO and other agencies to enhance access. Medicines included in the list
of essential medicines are those that satisfy priority needs of the people, selected on the basis of efficacy, safety and cost-effectiveness. Using only the list of essential medicines for procurement and by using pooled procurement, one government has reduced expenditure on medicines by 30% and these savings have been used to procure additional medicines. This has resulted in enhancing access to medicines in that 90% of the medicines in state hospitals are now actually provided free to the patients and are of good quality (16).

**Box 4: Responsibilities of physicians in ensuring access to medicines**

- As professionals, doctors are not expected to have any other overriding consideration than providing the best service to their patients.
- Physicians should, wherever possible, rescribe medicines included in the lists of essential medicines, which are prepared and regularly updated as part of the effort to enhance access.
- Drugs included in the list are those intended to satisfy priority needs of the people, selected on the basis of efficacy, safety and cost-effectiveness.
- Physicians have an important role to play in the development of tools to facilitate rational prescribing and use of medicines.

Source: Plianbangchang S. (Regional Director, WHO/SEARO). *Equity and responsibilities in providing access to medicines: the roles of physicians, researchers, manufacturers and governments* (5).

Medicines should be prescribed using their generic names provided the quality of generic preparations is up to the required standard. When a brand name is used in the prescription, the generic name must also be given. Generic prescribing would reduce the amount paid by the purchaser. It is not ethical that a poor patient is made to purchase expensive brand-name medicines prescribed by the doctor when an equally effective generic medicine is available at a fraction of the cost. It is unethical because studies have shown that one of the most common causes of indebtedness in rural communities is the amount spent by a family on medicines. One bout of illness can take away a poor wage earner’s entire earnings for a month – very often, spent on unnecessary medicines or unnecessarily expensive
medicines. The prescriber has a big ethical responsibility here. This is particularly so because in countries of the WHO South-East Asia Region, the percentage of out-of-pocket expenditure for medicines is high. This means that the patient pays for the medicines, money that could well have been spent on food, clothing or education for the children. While this figure for out-of-pocket expenses as a percentage of total health spending was 15.3% for the USA, 10.62% for the UK, 15.5% for Canada and 12.6% for South Africa, it was 82.2% for India (17).

A patient expects the doctor to be reasonably up-to-date and abreast of therapeutic developments and advancements. It is not ethical to prescribe medicines that are not currently used. The marketing company should withdraw these medicines. Although the regulatory control of these products should be exerted by the regulatory authorities, by and large, this is not being done. It is therefore the doctors’ and the prescribers’ responsibility to keep abreast of advances and prescribe accordingly. In several countries of the Region, due to weak regulatory control, drugs not approved or drugs removed from the list of approved medicines are still available in the market. Prescribers have a moral obligation not to prescribe these medicines for their patients. The physician should not depend solely on the medical representative for knowing about specific medicines, as this information could be biased towards the medicine being sold by representative’s company. Unfortunately, in many countries in this region, this is the only means available for a large number of doctors, to obtain information about new medicines. Doctors and other prescribers have to read objective and truthful information about medicines. Today, unlike 10 to 20 years ago, such information is readily available in the form of national and hospital formularies, drug bulletins and publications of drug information centres. The WHO Model Formulary gives independent information on essential medicines in the WHO model list.

Prescribers should not prescribe unnecessary medicines. This could lead to drug interactions and iatrogenic causes of morbidity and mortality in hospitals and higher costs of treatment. Elderly persons
are particularly sensitive to the side effects of medicines. In Norway, it was shown that 18% of all deaths of elderly patients in hospital were caused by medicines. Of these, at least 50% were avoidable (18). Prescribers should therefore be particularly cautious when prescribing for elderly patients.

Another result of indiscriminate prescribing is the development of resistance. This is particularly evident in the prescribing of antibiotics in the general population. Sometimes, it has been demonstrated that antibiotics form 32%-80% of all drugs prescribed (19). This type of reckless prescribing is unethical on the part of the prescriber, and results in development of resistance and also necessitates the use of second-line medicines, which are more expensive and may also be more toxic.

Prescribers need to prescribe rationally but very often pressures such as pharmaceutical marketing pressure, peer pressure and even patient pressure for a particular medicine or a new medicine that has been publicized in the lay press, can influence the prescribing habits of the prescriber.

Disciplinary action needs to be taken against health professionals when they are found wanting and guilty of unethical behaviour. This can be done by the government and the state medical councils. The latter may need to be strengthened for this purpose.

6.2 Medical education and the continuing education programme: tools for rational prescribing

Prescribers with experience and expertise have an important role to play in the development of tools, which are essential for rational prescribing. This includes modules on the rational use of medicines that can be included in the undergraduate curriculum of doctors, pharmacists and nurses. In addition, experienced prescribers need to give their time and expertise to the preparation of lists of essential medicines for different levels of health care, hospital and national
formularies and standard treatment guidelines. Prescribers, together with representatives of the pharmaceutical companies, need to follow or prepare a code of conduct for the relationship between the medical profession and the pharmaceutical industry. There are tools which will help to ensure access to medicines for the poor and the needy. In addition to preparing these tools, physicians should train persons to use them suitably, and see that they are used to encourage the rational use of medicines. WHO has sponsored and is sponsoring a number of training programmes on the rational use of medicines in the Region.

6.3 Providing information to the patient and the public

It is the responsibility of the prescriber to inform the patient about the medicines that have been prescribed. It is certainly not ethical to prescribe a number of medicines to a patient and not even tell him or her when or for how long these should be taken. A recent study undertaken at one of the government hospitals in a country in the WHO South-East Asia Region demonstrated that only 27% of the patients to whom medicines had been prescribed could answer two of the following three questions correctly when leaving the hospital with the medicines. The questions were:

- for how long will you take the medicine?
- how many medicines will you take?
- at what time will you take the medicines?

If only 27% of the patients knew two out of three answers (20), no wonder it was estimated that 50% of the patients did not take their medicines properly (2). Medical doctors and paraprofessionals prescribing and dispensing medicines have a responsibility to spend at least a few minutes to inform the patient about the medicines prescribed. This information should include not only the correct use of the medicines but also the precautions that may need to be taken, the possible common side effects and how to deal with them and
other commonly used medicines that may interact with the prescribed medicine to produce adverse effects.

Empowerment of the people to enable them to look after their own health will have to be included in educational programmes. An important component of such a programme is to provide information to the public. The prescriber, particularly if he is a medical doctor, should undertake social responsibility and talk at public meetings, whenever invited, on the proper use of medicines. An extension of this would be for the doctor with an interest and experience in rational prescribing to write articles in the popular press providing objective information about medicines and their rational use.

6.4 Links with the national drug regulatory agency

One point needs to be made about the ethics of a doctor who is undertaking a clinical trial of a new drug. The data of the trial belongs to the investigator who should be free to publish the results obtained. Any constraint on his/her right to publish results, which sometimes happens if the new drug is ineffective or induces unexpected side effects, would be regarded as unethical conduct by the pharmaceutical company if it insists that no publication should be made. The investigator should decline such an agreement. Withholding such information may be harmful to the public. The government has an ethical responsibility to regulate the pharmaceutical sector and to enforce regulation.

6.5 Responsibilities of the medical profession

Ethics and trust are the cornerstones on which the doctor-patient relationship has functioned for ages. Unfortunately, this is breaking down today. Patients have a feeling, justified in some cases, that doctors overcharge, keep them in hospitals longer than necessary, subject them to unnecessary tests, receive a proportion of the fees of the diagnostic laboratories and prescribe medicines not needed or expensive medicines because they are receiving favours from the
pharmaceutical companies concerned. Doctors need to regulate themselves fairly and in a transparent manner through the medical councils. If this is done, the old relationship of trust and empathy could replace that of doubt and suspicion. The relationship between doctors and the pharmaceutical companies must follow codes of conduct such as those framed by several professional bodies and by several medical councils. The codes clearly specify what is acceptable and what is not acceptable. Doctors should not undertake to carry out work in an area in which they have not been trained. For example, a doctor with expertise in diabetes or thyroid disorders should conduct trials in these areas. A doctor who participates in a multicentre clinical trial of a new drug without understanding the concept and practice of sample size, placebo, randomization and blindness is not behaving ethically. An additional role for doctors is to educate the patients and the public on the proper use of medicines. One cannot gloss over the fact that it is irrational prescribing of antibiotics, anti-tuberculosis medicines, etc. that has produced resistance to these medicines leading to the use of more expensive alternatives.
The major role of the government is to ensure equity. In order to do so, the government has ethical responsibilities in areas of drug policy and regulation, promoting the rational use of medicines, enhancing access to medicines as needed, particularly in the remote areas and for those who are underserved. It is also a major role of the government to provide and support training activities.

7.1 Drug policy and regulation

The government needs to develop a drug policy which includes ethics, equity and transparency and disseminate it widely throughout the country. Only medicines that are needed should be allowed to be marketed. The government should ensure that the essential medicines for the public sector are procured by the most effective system known today – pooled procurement – and distributed efficiently to all corners of the country. This is clearly the duty and the responsibility of the government. These medicines should be properly stored and prescribed rationally. Around this essential and important objective, several other regulatory and training activities need to be undertaken. Medicines not approved for use in the country should be removed from the market. A system of quality assurance should be set up to ensure that the drugs are of a high quality. Fake and substandard drugs should be removed from the market aggressively. It is also the duty and responsibility of the government to protect the public from unjustified and unethical advertising of medicines. This is easier said than done and laws may have to be strengthened or, if they do not exist, formulated. This applies equally to the visual, print and electronic media.
The government also has the responsibility of ensuring that the prices of medicines are kept at an affordable level. There are various ways of achieving this outcome. One way is to provide tax exemptions for special categories such as life saving medicines. Cost minimization – choosing an equally effective medicine with a lower cost through cost comparison analysis – is another way.

7.2 Enhancing access to essential medicines and adequate drug treatment

Although considerable progress in terms of access to essential medicines has been made in the last 25 years since the introduction of the essential medicines concept (Figure 1), not all people have benefited equally from improvements in the provision of health care services, or from low cost, effective treatments with essential medicines. Through a combination of public and private health systems, nearly two-thirds of the world’s population is estimated to have access to effective treatments with the medicines they need, leaving one-third without regular access. It is estimated that by improving access to essential medicines and vaccines, about 10 million lives per year could be saved (2).

*Figure 1: Estimates of the total number of people with access to essential medicines from 1977-1997 (latest available estimate)*

Source: Equitable access to essential medicines: a framework for collective action (21).
The government needs to play a coordinating role to ensure that all stakeholders carry out their responsibilities in the ethical use of medicines. In addition to developing and enforcing regulatory practices, the government will need to play a major role in the application of ethical principles in drug donations in a crisis situation. In this regard, Guidelines for Drug Donations prepared in collaboration with seven UN agencies and eight international nongovernmental organizations were published by WHO in 1999 (22).

It is important for the government to set up a system for monitoring the use of medicines, including setting up of pharmacoepidemiological studies, to know how medicines are being used in the country. This would undoubtedly promote the rational use of medicines benefiting the community.

Access to health care and therefore to essential medicines is a part of fulfilling of the fundamental right to health. All countries have to work towards equitable access to health services and commodities, including essential medicines necessary for the prevention and treatment of prevalent diseases. Appropriate policies and action plans need to be put in place to achieve this aim (Box 5).

**Box 5: Key points for policy makers: access to medicines is supported by the principles of the essential medicines concept**

- Common health problems for the majority of the population can be treated with a small number of carefully selected medicines.
- Individual health professionals routinely use fewer than 50 different medicines; the WHO Model List of Essential Medicines contains about 300 active substances.
- Training and clinical experience should focus on the proper use of these few medicines.
- Procurement, distribution and other supply activities can be carried out most efficiently for a limited number of pharmaceutical products.
- Patients can be better informed about the effective use of medicines by health professionals.
The access framework

Improving access to essential medicines is perhaps the most complex challenge for all actors in the public, private and NGO sectors involved in the field of medicines supply. They must all combine their efforts and expertise, and work jointly towards solutions. Many factors define the level of access, such as financing, prices, distribution systems, appropriate dispensing and use of essential medicines. WHO has formulated a four-part framework to guide and coordinate collective action on access to essential medicines (Figure 2). This framework has also been adopted by WHO’s key partners.

**Figure 2:** Estimates of the total number of people with access to essential medicines from 1977-1997 (latest available estimate)

The government needs to promote a programme of rational use of medicines together with the programme to enhance access (Box 6). This would be along the lines developed over the years by
The Role of Ethics in the Rational Use of Medicines

The World Health Organization and would contain the following elements:

- selection of lists of essential drugs for different levels of health care
- procurement by the government of only those drugs on the list by a system of pooled procurement
- setting up a good drug quality assurance system
- an efficient distribution system
- rational prescribing of medicines.

This programme by the government would improve therapeutics, reduce costs and provide an ethical framework for use of medicines in the country.

Box 6: Responsibilities of governments towards their citizens in improving access to medicines

- Health care is one of the most important fundamental requirements that citizens expect from their governments.
- The key role of the government is to develop measures to ensure equity in access to medicines by all who need them.
- The government should encourage medical and public health institutions and professional societies to organize training and education programmes aimed at enhancing access to medicines.
- The government needs to develop a robust drug policy based on the principles of ethics, equity and transparency.
- The curricula for health service providers need to be reviewed and revised to include components, which would enable these health staff to ensure access to medicines.

Source: Phamhongchang S. (Regional Director, WHO/SEARO). Equity and responsibilities in providing access to medicines: the roles of physicians, researchers, manufacturers and governments (5).

There are several other measures that the government could take to promote the rational use of medicines. These include proper post marketing surveillance of medicines to detect side effects, close
monitoring of the use of certain medicines such as those used for HIV/AIDS, TB, and urinary tract infections to improve compliance. There are also medicines with a high potential for misuse such as cough syrups, abortion pills now widely accepted to induce medical abortion, psychotropic medicines, and teratogenic drugs to ensure that they are not prescribed to pregnant women. One simple but important measure, which would make a big difference, is for the government to ensure that all the dispensed drugs are labeled appropriately.

In providing information to the public, the government should immediately inform the prescribers and the public if a medicine is being withdrawn from the market because of an unacceptably high incidence of side effects. The government also needs to provide objective and unbiased information about medicines to the medical practitioners and also about proper use of medicines to the public.

7.3 Clinical trials registry

There has been for several years, an expressed need for public registration of clinical trials and reporting of clinical trial results. There are a number of clinical trial registers being used in patient recruitment, investor information, research funding, etc. However, these registers are not complete or comprehensive enough for decision makers, researchers, research funders, policy makers, medical practitioners, patients and the general public to help guide research or make treatment decisions.

In May 2005, the Fifty-eighth World Health Assembly adopted a resolution (WHA58.34) on the Ministerial Summit on Health Research held in Mexico in 2004. One of the recommendations of the ministerial summit was to establish the International Clinical Trial Registry Platform that will set international norms and standards for clinical trial registration and reporting. The primary objective of the Registry Platform is to ensure that all clinical trials are registered and thus publicly declared and identifiable so as to ensure that for all trials, a minimum set of results will be reported and made publicly available. This will further improve good research practice, assist in
making treatment decisions, and help increase public trust in clinical research.

Member States were urged, among others, to contribute to the development of health research by committing funds for necessary health research to reduce inequity and social injustice. Also, to promote activities in strengthening national health-research systems including improvement of the knowledge base for making decisions, setting priorities, managing research, monitoring performance, adopting standards and regulations for high-quality research and its ethical oversight; and ensuring participation of the community, nongovernmental organizations, and patients in such activities (23).

### 7.4 Training activities

No programme aimed at enhancing access to adequate treatment can succeed without extensive training programmes and continuing medical education programmes. The government should encourage medical institutions and professional societies to organize such training programmes. Logistics of procurement, storage and distribution of drugs and rational prescribing would be important topics for such courses. The undergraduate curriculum for doctors, nurses and pharmacists needs to be revised to include modules which would enable these categories of personnel to help in enhancing access to medicines. Another important area would be to train professionals and paraprofessionals in the proper use of medicines of immense public health importance such as anti-retroviral medicines for HIV/AIDS.

No training can be carried out without policies and tools. These include lists of essential medicines, standard treatment guidelines particularly for the use of medicines in national programmes, national and hospital formularies, medicine information sheets and relevant manuals on rational prescribing and procurement, storage and distribution of medicines. If these do not exist, the government should either publish such manuals themselves or encourage other organizations to develop them. Guidelines are specially needed for use of medicines in children and the elderly.
The government should also sponsor research in the field of medicines, including the areas of health systems research to increase access and rational use of medicines, particularly among the poor. It also needs to develop a strategy for capacity building in the relevant areas. In this effort, the strategy of empowering people to look after their health by educating them should be kept in mind.

The responsibilities and obligations of the government are many. These include:

- removal of all unapproved drugs from the market;
- carrying out an aggressive programme to eliminate counterfeit drugs circulating in the country;
- taking legal and punitive action against unjustified claims for medicines and modify existing legislation if necessary;
- ensuring that prices of medicines are kept at a reasonable level. Whenever possible, tax should be levied on non-essential medicines;
- ensuring that drugs are labeled properly and that the labeling is not misleading;
- revise the undergraduate medical, nursing and pharmacy curricula to include modules on the rational use of medicines;
- disseminate widely the drug policy of the country after formulation or revision;
- set up a wide network of quality control laboratories throughout the country and ensure a system of quality assurance of medicines;
- establish units for promotion of rational use of medicines in all Departments of Health;
- empower people to look after their own health through public meetings and establishing drug information centres at selected locations;
• organize training programmes for doctors and other health professionals;

• develop subsets of lists of essential medicines for the elderly and children;

• set up monitoring units to document the use of medicines with a high potential of misuse such as cough syrups, abortion pills and psychotropic medicines;

• assess the benefit/risk ratio of new medicines and the cost impact of new medicines before releasing them on the market;

• set up an accreditation system for all centres carrying out clinical trials of new drugs;

• maintain a registry of all clinical trials being carried out in the country which could be in the public domain.

While some of the above responsibilities and obligations of the government are more important than others, all contribute to equity, access and rational use of medicines.
There is a need to ensure the application of ethics in public health as this is often a neglected area. Four topics are highlighted in this section.

### 8.1 The multilateral agreement on Trade Related Aspects of Intellectual Property Rights (TRIPS)

The TRIPS Agreement has provisions for compulsory licensing and parallel importation. They are reiterated in the Doha Declaration, thus enabling promotion and marketing of generic drugs at affordable prices. Some bilateral and regional free trade agreements now being entered into contain what have been described as TRIPS-plus provisions. These provisions restrict options for compulsory licensing and parallel importation, extend the period of data exclusivity after expiration of patent, prevent national drug regulatory authorities from granting marketing approval for generic products without consent or agreement of the patent holder, etc. These issues will reduce or prevent availability of lower priced generic medicines. In the interest of equity and social justice, countries should not accept any “TRIPS-plus” provisions which limit their right to use all available flexibilities contained in the TRIPS agreement. It would be in the interest of the developing countries to negotiate Intellectual Property Rights (IPRs) at the multilateral level to obtain safeguard what has been achieved (24).
8.2 Donation of medicines in emergencies

The humanitarian response to any disaster is to help with donation of food, clothing, shelter and medicines to relieve suffering and to bring comfort and solace to those in need. Unfortunately, there are many problems associated with donation of medicines such as irrelevance to needs, inability to understand the language in labeling, doubtful quality of medicines, high declared value and inappropriate quantities that often necessitate destruction and disposal resulting in wastage.

The post-tsunami donations of medicines in Banda Aceh province in Indonesia highlighted once again the need for ethics in donation of medicines and ethical failure in emergencies. By early 2006, significant volumes of outdated or obsolete medicines had accumulated in quantities estimated to be in thousands of kilogrammes (25). The local authorities described the conditions of the donated medicines as follows.

- Expired/outdated medicines. These stocks were either outdated when delivered, or became outdated soon after their delivery or will become outdated before their probable use; e.g. Diagyl (expiry December 2002), Kemygyl (expiry July 2004), etc.

- Unnecessary products: products for which there is no use; e.g. levofloxacin-cefotaxime (not listed in national essential medicines list).

- Labeled in foreign languages that cannot be understood by local staff; e.g. 10 boxes of medicines labeled in Chinese, medicines from Poland and Ukraine.

- Products not registered in Indonesia; e.g. expectorant syrup from India.

- In excess of needs: some products have been supplied in quantities that would meet the needs of the entire Banda Aceh population for ten years; e.g. Ringer lactate solution, amoxicillin 500 mg.
- Products deteriorated through poor storage conditions: in direct sunlight or at high temperature; e.g. aspirin, amodiaquine, aminophylline, amoxicillin syrup, ampicillin vial.

The Guidelines for Drug Donations (22) has enunciated four core principles for improving donations of medicines (Box 7).

**Box 7: Core principles for donation of medicines.**

1. Maximum benefit to the recipient.
2. Respect for wishes and authority of the recipient.
3. No double standards in quality.
4. Effective communication between donor and recipient.

### 8.3 WHO and civil society collaboration

Even though medicines are used by an individual, it must be seen in the context of the family, the community and society as a whole. The taking of medicines by an individual can be influenced by his/her own family often without having proper information. Neighbours and the community in general may also influence the medication of the individual through their own perception of the medication and not based on medical knowledge. Unqualified persons dispensing medicines, even giving injections, in rural and remote areas, compound the problem of improper use of medicines.

To curb such inappropriate practices, civil society as a whole needs to play an important role. This could be achieved by developing public and patient education strategies on appropriate use of medicines. There is a need for increasing awareness for educating the public; a better understanding of behavioural and social determinants of using prescription medication or self-medication;
expanded coverage by the mass media and communication technology and improving access to objective and understandable information.

8.4 Role of the media

The media can play an important role in influencing the proper use of medicines. This includes providing objective, correct and precise information and avoiding sensationalizing, or contradiction. Any information requested by the media should be given by an authorized source such as the Department of Health or the drug regulatory authority through press releases to avoid misquotation. The media should contribute to increasing awareness of the community regarding problems in the use of medicines.
The strategies to improve the rational use of medicines must be based on identification of problem areas as well as prioritization of issues and activities that would improve the use of medicines effectively and efficiently.

9.1 Identification of problem areas

The many stakeholders involved in the rational use of medicines chain of events need to display ethical responsibility. It is necessary to identify the points at which matters can go wrong. The challenges in medicines chain are given in Section 5.3. There must be constant monitoring of unethical practices and appropriate actions to be taken must be identified and publicised to reduce such practices.

9.2 Strategies for improving the rational use of medicines

Seven strategies for improving the use of medicines are highlighted below.

Professional conduct: A code of conduct should be laid down. All professionals should be encouraged to follow the code, which must be enforced by medical councils. Any violation should be punishable.

Researcher: Research should follow the principles of Good Laboratory Practice and Good Clinical Practice at the preclinical and...
clinical stages. Clinical trials should be carried out only after approval from the drug control authority and ethical review bodies.

**Drug development:** Medicines required by the country should get preference in development, an essentiality clause may be considered for orphan drugs and those specifically required for the country such as new antimalarials and antituberculosis medicines. Manufacturers should not focus only on life style and “me-too” medicines.

**Pharmaceutical industry:** The pharmaceutical industry must provide appropriate, correct and timely information to the medical and allied professions for every medicine introduced in the market.

**Regulation:** Regulatory control must be a component of drug policy that emphasizes the aim of rational use of medicines which includes ethics, equity and transparency. Only registered medicines should be allowed to be marketed. Regulation should be enforced to ban drugs not approved for use in the country. A sound system of quality assurance must be ensured and substandard drugs must be removed from the market. Promotion of medicines should be especially regulated.

**Rational use of medicines:** It must be ensured by using a limited list of generic medicines with assured quality, bulk procurement and established medicine chain. Training in these areas can improve the rational use of medicines.

**Marketing:** Medicines should be marketed only after approval by the drug control authority. No monetary incentives should be given for this approval. Compulsory reporting of side effects seen in post-marketing surveillance should be built into the marketing permission of the pharmaceutical company.
The rational use of medicines has a strong component of ethics and equity. Different segments of civil society and governance must recognize it as such. When people have the right to medicines, and when the resources and technology are available, then it is unfair and unethical for the people to be deprived of the benefits of medicines.

The ethical responsibilities of four sets of players have been delineated in this document. They are the researchers in their quest for discovery of new drugs, manufacturers of pharmaceuticals, members of the medical and allied professions and the government. If these four sets of important players realize their responsibilities and try to improve access to essential medicines and their rational use within the framework of ethics and equity, then the situation is certain to improve. It is with this hope that The Role of Ethics in the Rational Use of Medicines has been prepared.
References


7. Consolidated list of products whose consumption and/or sale have been banned, withdrawn, severely restricted or not approved by Governments. New York, United Nations, 2003 (ST/ESA/282).


25. Hilderbrand AV. Personal communications in 2006. Food and Chemical Safety Unit, New Delhi, WHO Regional Office for South-East Asia.
The Constitution of the World Health Organization states that, “The enjoyment of the highest attainable standard of health is one of the fundamental rights of every human being…. “ Access to essential medicines and their rational use are crucial elements in the delivery of health services and health care and can be seen as a part of the fundamental right to health.

This publication highlights the need to observe ethics and codes of conduct by four entities associated with medicines. The researcher who is concerned with the development and discovery of drugs; the pharmaceutical manufacturer who is involved in the development, production and promotion of medicines; the medical and allied professionals who prescribe, and dispense them and the government who is responsible for the regulatory control of medicines.

Strategies to improve the use of medicines have also been delineated. They are:
(1) institution of regulations based on ethics, equity and transparency;
(2) research based on Good Clinical Practice;
(3) drug development based on needs of countries including orphan drugs, antimalarials and anti-tuberculosis medicines;
(4) marketing to be coupled with post-marketing surveillance for regulation of medicines and
(5) ethical principles observed by all stakeholders in the medicines chain which includes research and development, clinical trials, registration, manufacturing, patents, prices, distribution, donations and promotion.

Ethics should form an indispensable component of the strategy for promoting the rational use of medicines.

Department of Health Systems Development
Essential Drugs & Medicines (EDM)
World Health House
Indraprastha Estate
Mahatma Gandhi Marg
New Delhi 110002
India

Telephone: +91-11-23370804, Fax: +91-11-23370197
Email: edm@searo.who.int,
Website: http://www.searo.who.int/en/section1243.htm