International Federation of Associations
of Pharmaceutical Physicians
founded 1975

INTERNATIONAL CODE OF ETHICAL CONDUCT FOR PHARMACEUTICAL PHYSICIANS

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Preamble

Medical ethics have been governing human behaviour as far back as 460-357BC. However as science becomes more innovative and medical research processes more creative, the ethical boundaries that limited “what was considered possible” are now being challenged by scientific endeavour using rational justifications that often go beyond common sense.

The revised Declaration of Helsinki, the EU Clinical Trial Directive, and the Washington Post "Body-hunters" series from December 2000, are just a few of the controversial “ethical” issues that inevitably opens the pharmaceutical industry to ever increasing public scrutiny. Dialogue amongst patients, investigators, institutions, sponsors and the media, –“60 minutes” and “Larry King” highlights the need for transparency, and guidance on how Pharmaceutical Physicians as ‘the conscience and guardians” of Pharmaceutical Ethics can pro-actively manage these situations responsibly, well before they become major issues.

An International Working Party [WP] was established in September 2001 to advise The International Federation of Associations of Pharmaceutical Physicians [IFAPP] on how to manage this complex area. It recognized that there are ethical issues, which are of particular relevance to Pharmaceutical Physicians and believes that it has a responsibility to define and publish standards to which Pharmaceutical Physicians and others can refer.

This code deals principally with those ethical issues that might face a Pharmaceutical Physician, whether he or she is practicing within a company, a contract research organization, as an independent consultant, in an academic department, a regulatory authority or elsewhere, and seeks to offer guidance and support. It is intended to be a living document, to be regularly reviewed and updated as issues arise or are solved.

There is a need for an International Ethics Network of Pharmaceutical Physicians working on such issues, taking into account the progress achieved within therapeutics, the work already achieved by others in the field of bio-ethics and the texts already published. Pharmaceutical Physicians are essential members of the teams working throughout the life cycle of a therapeutic intervention, from the discovery research phase, through pre-clinical and clinical testing, licensing, launching, post-marketing studies and surveillance, through to its eventual demise whether on grounds of relative safety and efficacy or commercial non-viability. Being members of a team there is an understandable tendency for Pharmaceutical Physicians to develop a strong interest in an intervention with which they have had a long or close association. Despite this, Pharmaceutical Physicians should recognize their ethical responsibility and stand aside from product loyalty when assessing factors affecting the product itself. They must remain aware at all times that the ultimate interests of both patients and their own employers are best served by an objective scientific attitude. The IFAPP recognizes that this may place a practicing Pharmaceutical Physician in a position, which demands considerable determination.

Ethics plays a vital role in enabling Pharmaceutical Physicians to situate their professional lives with their personal, communal, philosophical and religious lives. All clinical development activities and medical support services must therefore be provided by appropriately trained individuals working to agreed standards in adequately staffed departments with clear responsibilities and the authority to take necessary decisions. Accreditation of Pharmaceutical Physicians is an essential element of the demonstration of appropriate training in Pharmaceutical Medicine. As in all branches of medicine, accreditation should not be seen as a single event but as subject to re-validation, as this becomes available. Further, medical ethics does not yet feature prominently in the syllabuses of all medical schools throughout the world, yet it is increasingly recognized as important. It follows that training in Ethics in Pharmaceutical Medicine is itself important for all Pharmaceutical Physicians, health professionals, research ethics committee members and others involved in the research and development of therapeutic agents. The IFAPP recommends that this should feature in the various training courses provided for individuals seeking recognition as Pharmaceutical Physicians. By this means the achievement of professional excellence can be fostered and self-identity and professional aspirations supported.

Pharmaceutical Medicine is a discipline that involves the discovery, development, evaluation, registration, monitoring and ethical marketing of medicinal products, medical devices and diagnostics. However, the users of healthcare products are not necessarily aware of the costs and complexities involved in the development and registration of a therapeutic intervention, and of the issues possibly arising throughout its subsequent existence. Pharmaceutical physicians have a responsibility to raise awareness and understanding of the different pressures and constraints governing healthcare products.

Member nations are invited to review this document, and provide feedback. Please address your comments to the Working Party

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The Code Explained

This International Code of Ethical Conduct for Pharmaceutical Physicians has been drafted making the fundamental assumption that Pharmaceutical Medicine and Pharmaceutical Physicians across the globe embrace the following core values in the ethical discharge of their duties: the values of Duty of Care [Good Clinical Practice], Competence and Diligence, Impartiality, Probity, and Integrity and Accountability in the Workplace.

The Structure of the proposed Code names and introduces the Core Value, then lists Specific areas of ethical concern for Pharmaceutical Physicians.

The hope is that the code, following worldwide consultation, will be both relevant and universal, and be adopted in most parts of the world. Similarly it may stimulate those countries that have not yet adopted a Code of Ethical Conduct to consider such an approach.

Only in this way can standards and values in Pharmaceutical Medicine become universally accepted. However it would be presumptuous to believe that acceptance of this Code could supersede the national sovereignty rights of any nation, however at best could be highly influential, and a model worth considering.

Duty of Care

Good Clinical Practice

Pharmaceutical physicians are required by the nature of their job to keep themselves abreast of scientific advances that will have a major impact on the development of the new medicines of the future. A registered medical practitioner with appropriate special training should be in overall control of any research involving human subjects. This must include training in medical ethics and up to date best practices.

Specific areas of ethical concern for Pharmaceutical Physicians:

- Ensuring that they remain well informed about current scientific and medical knowledge in the areas of therapeutics in which they work.

- Maintaining the high standards required by national and international regulations.

- Assimilating constructive feedback from management, internal review committees, ethics committees and the regulatory authorities.

- Designing clinical research programmes and protocols in areas of medical need according to regulatory requirements, national and international codes of practice, and the declaration of Helsinki.

- Ensuring that they fulfil their obligations in clarifying, evaluating and reporting adverse events, whether they come from research protocols, spontaneous reports or as part of a formal surveillance programme.

- Ensuring that documents submitted to the regulatory authorities accurately reflect the data that have been gathered in the development process.

- Ensuring that relevant data are made available for publication and that articles submitted to journals accurately reflect the data on which they are based.

- Passing of accurate and verifiable information to the company's sales department.

- Teaching, training, appraising and assessing of other members of the medical department.

Medical Integrity

Research involving the use of people as study subjects may be justified under certain circumstances but only after careful consideration of the risks and benefits involved. The health and well being of each such study subject is of paramount importance and relegates all other considerations to being of lesser importance. People volunteering to be study subjects, both healthy volunteers and patient volunteers, are required to give written informed consent after receiving sufficient and properly witnessed explanations of any potential risks and benefits involved. Particular care must be shown when studies include patients who are not volunteers and cannot give consent for themselves, whether due to their age (children) or lack of capacity (the unconscious or mentally incompetent for example). Financial compensation should be appropriate without constituting exploitation, coercion or bribery, and should have been discussed with the ethical review committee.

Specific areas of guidance for Pharmaceutical Physicians:

- Clarifying whether or not the company will provide continuation of support and interventions once a patient's involvement ends and the mechanism by which this will occur.

- Ensuring that in the provision of disease management packages any conflict between competing interests is minimized, for example where the treatment of choice may be a therapeutic agent produced by a competitor.

- Ensuring that the best interests of individual patients always prevail over those of the employer.

- Utilising individual clinical judgement over management guidelines where it can be demonstrated that an alternative course of action is more appropriate for an individual patient.

- Ensuring that information is provided in accordance with the principles of evidence-based medicine to optimize the acceptability of products for which they are responsible, but within appropriate clinical management guidelines.

- Resisting the use of therapeutic interventions outside of clinical management guidelines without conducting appropriate clinical trials and/or obtaining the necessary regulatory clearance.

- Reviewing local guidelines with regard to the payment of patients in clinical trials, and ensuring that local ethical committees/institutional review boards are informed and consulted.

- Ensuring that patients are not inappropriately induced to take part in clinical studies.

- Respecting their duty of care regarding the use of unlicensed or unproven interventions, regardless of the source.

- Assuming responsibility for any patients under their care, whilst the providers of the interventions carry responsibility for the quality of whatever they supply.

- Ensuring that patient information leaflets are clear and can be understood by the end user.

Competence and Diligence

General issues in clinical research

Intentions to perform research on humans must be carefully thought through. The person in overall control must ensure that the scientific approach is current and the methodology is good, the motivation is clear, the processes are unambiguous, and sufficient data exist to judge the safety and effectiveness of interventions proposed.

Specific areas of ethical concern for Pharmaceutical Physicians:

- Ensuring that the study site chosen for a study, the chief investigator at the site and the entire support staff should be appropriately equipped and trained to properly care for each study subject participating.

- Remembering that it is unethical to change from an effective treatment to a trial medication unless there are sound scientific reasons for doing so, approval is obtained from a research ethics committee, the appropriate explanation is given to any trial subject and consent obtained.

- Ensuring that scientific and ethical standards are constantly upheld.

- Selecting appropriate investigators prior to the start of a clinical trial, and ensuring that they are trained to recognisably appropriate levels.

- Making a clear statement of the sponsors' policy with regard to the handling of suspect data.

- Resisting undue pressure on any investigator in order to meet deadlines.

- Familiarising themselves, and staff, of the policy and standard operating procedure in place relating to the management of suspected fraud, and demonstrating commitment to implementing the policy if occasion demands.

- Ensuring that sufficient data are generated to allow the safe and effective use of a therapeutic intervention.

- Ensuring that studies are designed primarily to demonstrate the properties of the therapeutic agent under study rather than those of any comparators.

- Ensuring that studies involve placebos only when it is ethically appropriate to do so.

- Providing research ethics committees with all relevant information to enable them to make a considered judgement on the ethics of any given research protocol.

- Ensuring that payments for studies, details of the recipients, and potential conflicts of interest, are totally transparent and revealed to research ethics committees.

- Ensuring that policies that safeguard the interests of research subjects, in terms of indemnity and compensation, are clearly in place.

- Remembering their duty to apply standards of scientific rigour and provision of quality information wherever they may be working, be it in research, production or marketing.

Studies of human pharmacology

Specific areas of ethical concern:

- Providing non-patient volunteers recruited into human pharmacology or phase I studies with summaries of all-important and relevant findings on the therapeutic interventions.

- Ensuring that volunteers recruited from among employees of the sponsoring body, or among students, are not exploited, coerced or inappropriately remunerated.

- Ensuring no conflict of interest between those who design studies, including human pharmacology or Phase I studies, and the teams responsible for their implementation.

- Obtaining independent ethics committee approval for all clinical studies.

Studies of therapeutic use and post-marketing surveillance

Once a therapeutic intervention has reached the stage where it is available for use, pharmaceutical physicians have an ethical responsibility to ensure that any studies they design, whether as observational post-marketing surveillance studies or as therapeutic use trials, will provide information regarding appropriate use in real life situations.

Specific areas of ethical concern:

- Ensuring that no marketing exercise ever masquerades as a scientific study, be it a clinical trial or an observational post-marketing surveillance study.

- Paying due regard to the need for guidance on hypothesis generation and confirmation for such studies.

- Ensuring that the handling of observational databases and extracting of interpretations from them be of the highest standard.

- Contacting the sponsor of a study if, despite the approval that will have been given by a relevant research ethics committee, a pharmaceutical physician comes across a potentially unethical study being conducted by another person.

Special and vulnerable patient groups

This group includes children, the elderly, the mentally incompetent, the mortally ill, the unconscious, the disadvantaged, prisoners etc., These groups should not be deliberately excluded from clinical studies as to do so may cause them and others in their condition more harm. But if they are to be included then very special circumstances apply and should be followed carefully. If such people are the intended beneficiaries of the interventions under study, sufficient must be known about the interventions to make a risk versus benefit

judgement possible. This usually means that data from prior work on adults able to give informed consent will have been completed and is available for review.

Children

Specific areas of ethical concern:

- Ensuring that the local ethical position regarding the use of children in research projects is clearly understood.

- Ensuring that where a therapeutic agent is not intended for use in children then paediatric studies are not conducted.

Special risk groups

Specific areas of ethical concern:

- Ensuring that the local ethical position regarding the use of special risk groups (e.g. the elderly, the mentally incompetent, those with terminal or vital disease, those who are socially or economically disadvantaged, or any condition or circumstance where informed consent may not be obtained easily) is clearly understood.

- Clearly understanding the local ethical position regarding non-therapeutic trials without direct benefit to the patients involved (e.g. those with hepatic or renal impairment).

Research in less developed countries

The locally prevailing social attitudes must be seriously considered when contemplating studies using volunteers from less developed and developing areas of the world. Judgements of what is appropriate will vary according to social, ethical, economical and governmental factors, which are local and not necessarily international. The principles of beneficence and respect for human dignity prevail everywhere.

Specific areas of ethical concern:

- Ensuring that special care is taken to obtain local independent ethical review and approval, where the approval of an institutional review board in a developed country is not sufficient or relevant.

- Taking particular note of the ethnic, social, public health and economic conditions prevailing in the country concerned when any form of clinical research is being considered.

- The use of placebo controls in conditions where such controls would not be acceptable in the developed world.

Orphan indications and/or medicines

A particular ethical dilemma arises with regard to orphan indications and to orphan therapeutic interventions i.e. where too few patients have a disease for a treatment to be fully investigated in the usual way. There are some rare conditions for which it is clear that there will never be a viable commercial return on investment. In such circumstances the intervention may also not be assessable using the normal criteria.

Specific areas of ethical concern:

- Making limited information available to others about orphan conditions, such that they can give advice to patients or their families.

- Making ethical decisions that it may be better to recommend an orphan intervention than to deny anyone who might benefit from it.

- Making information available to the owners of the relevant therapeutic agents on the need for orphan medicines and their availability.

Benefit - risk assessments

If a pharmaceutical physician is not certain about all aspects of the status of a clinical research programme, even in the light of acceptable efficacy or safety, it is appropriate to delay making a decision on its future progress until any doubts have been resolved. Making an inappropriate decision before such doubts are resolved is unethical. Thus, both when assessing the outcome of a clinical trial programme and when reviewing the safety profile after marketing, pharmaceutical physicians must actively fulfil their scientific and ethical responsibilities.

Specific areas of ethical concern:

- Making forthright ethical decisions where the relative evidence of efficacy is less than acceptable or where there is an unexpectedly high incidence of adverse reactions.

- Ensuring that adequate systems are in place to ensure the timely capture and analysis of relevant data upon which a decision to withdraw or modify an intervention might be based.

- Balancing the potential benefit of a trial to a larger number of patients against the possible harm done to a smaller number.

- Ensuring, in the case of a withdrawal of any therapeutic intervention, that as much relevant information as possible is made available to enable the clinical care of patients who are affected by the withdrawal to continue with the minimum of disturbance.

- Appreciating that the evidence available to formulate a benefit-risk assessment increases with time as use of the new intervention increases, and utilising such information to reduce the time taken to achieve an optimum assessment of a benefit-risk profile.

Awareness of innovation

There are new technologies of which pharmaceutical physicians should be aware, such as pharmacogenetics and pharmacogenomics, which are used for selecting and classifying patients. In the design of research protocols using such tools, pharmaceutical physicians should be vigilant in protecting patient rights.

Specific areas of ethical concern:

- Understanding and respecting local regulations and conventions governing the collection, management and specific analysis of clinical data for which consent may not necessarily have been given (pharmacoepidemiology).

- Ensuring the maintenance of high ethical standards and fulfilment of all legal requirements when using electronic clinical data management.

- Maintaining awareness of controversial and new therapeutic approaches in the wider context of the practice of medicine where ethical issues arise e.g. the sampling and use of human body products (including organs, tissues, fluids or gametes), in-vitro fertilisation or other methods of medically assisted procreation where medicinal products may be involved, prenatal diagnosis, certain aspects of contraception and abortion, and the interface with medical devices and delivery mechanisms.

- The long-term storage of blood taken for genetic testing, and the consequences to the patients and their families of results from tests performed in the future.

Impartiality

Studies are performed to increase knowledge in some way, and this knowledge should be shared with the wider world. Study findings should be communicated, whatever the outcome, for the benefit of the community at large. Communications on clinical studies must be a correct representation of all the findings, allowing others in their turn to give well-balanced advice to patients and their families.

Promotion

Specific areas of ethical concern:

- Ensuring that any promotional material or activity does not contravene the advertising regulations and codes of practice of the countries concerned.

- Ensuring that Pharmaceutical Physicians do not allow claims to be made which they consider unjustified.

- Assuming the responsibility to ensure that market research and promotional research activities are not perceived as scientific research projects.

Provision of information

Specific areas of ethical concern:

- Ensuring that information provided to doctors, pharmacists, patients and members of the public is appropriate and accurate.

- Ensuring that patient information is detailed enough to satisfy legal and regulatory requirements, but which is not so detailed that it affects the confidence of a patient or their family in the product and therefore negatively affects compliance.

- Ensuring that products can be used appropriately in the target countries for which they are intended.

- Recognising that summaries of product characteristics exist not only to fulfil legal requirements, but also to help physicians to use products safely and correctly.

Information to healthcare professionals

Doctors are increasingly being encouraged to practice medicine based on all the available evidence in an attempt to improve further the quality of healthcare. Pharmaceutical Physicians have a particular ethical responsibility to ensure that all the evidence on which doctors should make their decisions is freely available. It is well recognized that doctors sometimes prescribe medicines for indications or in dosage regimens that are not in accordance with the terms of the product's marketing authorisation. Although there can be no question of promotion of interventions for such “off label” use, nor should this be encouraged, relevant information, which is on file, should be provided on request to physicians and pharmacists.

Specific areas of ethical concern:

- Ensuring that data to support marketing position statements should be of the same high quality, and conform to the same scientific criteria, regardless of whether they are published or unpublished.

- Encouraging the provision of all information known about an intervention to those entitled to it, regardless of whether or not this information has been published.

Information to patients

There is increasing freedom in the provision of information and the encouragement given to patients to seek as much information as they wish. This should certainly be permitted, but not so that it undermines the confidence of patients in the advice and treatment given by their own doctors.

Specific areas of ethical concern:

- Ensuring that there is a clear understanding of the difference between providing clear information to patients, and the offering of advice, which should come from their personal physician.

- Ensuring that patient information is detailed enough to satisfy legal and regulatory requirements, but which is not so detailed that it affects the confidence of a patient or their family in the product and therefore negatively affects compliance.

- Ensure that information intended for patients is appropriately directed and suitably written so patients and their families are able to make an informed decision about their treatment and medication.

Information to the media

Specific areas of ethical concern

- Ensuring that expectations are not inappropriately raised as a result of the release of media briefings.

- Reviewing briefings about potential therapeutic interventions provided to financial analysts or to the media.

- Drawing to the attention of the authorities the distribution of any medicine, for example via the Internet and websites, which bypasses national legislation.

Probity

Pharmaceutical physicians usually work for a commercially driven operation. They must, therefore, be extra vigilant that their decisions and practices are not in any way influenced by any personal financial gain. Each of the many players involved in planning, sponsoring and performing such studies must spontaneously declare potential conflicts of interest that might influence the making of balanced, unbiased judgements of what is best for study subjects.

Accurate reporting

Specific areas of ethical concern:

- Ensuring that final study reports accurately reflect the clinical data and that any publication that flows from the data is wholly consistent with the report.

- Maintaining the principle that all relevant reports should lead to a publication and not be persuaded by the argument that adverse data will have a negative impact on the finances of the company.

- Ensuring that all studies performed are analysed and have a report written, however brief, as not to do so means that valuable data will be lost and patients will have been

potentially put at risk for no benefit to themselves or others. This information should, wherever possible, lead to publication.

- Ensuring that advertising and promotional material is both legal and ethical.

- Balancing the need to make promotional material interesting and attractive against the need for scientific and medical accuracy.

- Ensuring that the commercial interest of a company is never allowed to take precedence over the requirement to report all safety data and adverse drug reactions to the authorities.

Research accountability

Specific areas of ethical concern:

- Designing clinical research protocols to answer genuine scientific questions and not to be promotional tools.

- Implementing a clinical research protocol only after the approval of an independent research ethics committee.

- Protecting subjects as a priority over scientific interest in all research protocols.

Financial and commercial dealings

Specific areas of ethical concern:

- Refusal to accept gifts or hospitality designed to influence professional judgement.

- Compensation for carrying out a clinical trial must be commensurate with the work required and not structured in such a way as to encourage coercive behaviour.

- Declaration of financial interests in dealings with professional colleagues, the editors of scientific journals and the general public.

- Payments for any reasons, to both volunteers and those performing the study must be transparent and known to the review body, as must any potentially conflicting interests.

- Arrangements for product liability, indemnity and compensation in the event of anyone suffering damage must be clear, both to review boards and potential study subjects.

Integrity and Accountability in the Workplace

Propriety

Specific areas of ethical concern:

- Ensuring that colleagues are always treated fairly and are not discriminated against in any way.

- Ensuring that a colleagues' lifestyle, culture, beliefs, colour, gender, sexuality, or age does not prejudice a professional relationship with them.

- Ensuring that subjects' trust in the care or treatment they receive, or in the judgment of those treating them, is not undermined by the malicious or unfounded criticisms of colleagues.

Teamwork

Multi-disciplinary teams increasingly provide pharmaceutical research. Working in a team does not change personal accountability for professional conduct and the care provided.

Specific areas of ethical concern:

- Respect of skills and contributions of colleagues.
- Effective communication with colleagues within and outside the team.
- Participation in regular reviews and audits of the standards and performance of the team.
- Willingness to deal openly and supportively with problems in the performance, conduct or health of team members.

Leadership

Specific areas of ethical concern:

- Ensuring that medical team members meet the appropriate standards of conduct and care.
- Addressing any problems that might prevent colleagues from other professions following guidance from their own regulatory bodies.
- Ensuring that all team members understand their personal and collective responsibility for the safety of patients, and for openly and honestly recording and discussing problems.
- Arranging for the provision of physician availability at all times.
- Regularly reviewing and auditing of the standards and performance of the team and addressing any deficiencies.
- Ensuring that systems are in place for dealing supportively with problems in the performance, conduct or health of team members.