

GUIDING PRINCIPLES FOR PHARMACEUTICAL PHYSICIANS

Ethical Issues Subcommittee of the Faculty of Pharmaceutical Medicine of the Royal Colleges of Physicians of the United Kingdom

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Medical practitioners practising in the field of pharmaceutical medicine, whether in industry, regulatory bodies or an academic environment, are bound by the same ethical standards which apply to all doctors. Their work, however, leads to some very specific ethical considerations which may not be fully explored in ethical codes based in clinical medicine.

This document aims to establish some guiding principles which should underpin a working ethical framework for pharmaceutical physicians. It clearly places the protection of patients (and research subjects) and the doctor's duties to the wider public ahead of responsibilities to an individual employer. It also emphasises the importance of medical leadership in promoting ethical principles and accountability in clinical decision making; adherence to objective decision making based on merit and high standards of research, including openness and honesty in the dissemination of findings.

This version of the Guiding Principles is derived from the original publication^{1a} and a full report^{1b} published in 2006. The full report offers more specific practical advice on possible ethical conflicts or dilemmas.

The three underlying principles that guide the protection of patients and research subjects...

① Individuals Come First

Although the aim of clinical research is to advance medical knowledge and practice, the health and well-being of patients and research subjects must at all times take precedence over the research.

② Confidentiality

Pharmaceutical physicians must treat information about patients and research subjects as confidential. If, in exceptional circumstances, there are good reasons why information should be passed on without consent, or against an individual's wishes, the process should follow the guidance of regulatory bodies and the decision to do so be justified.

③ Justification

Research involving the use of humans as study subjects, be they healthy volunteers or patients, may be justified under certain circumstances but only after careful consideration of the risks and benefits involved.

The Faculty of Pharmaceutical Medicine is a registered charity with approximately 1,400 members who are practising or retired pharmaceutical physicians or those with a professional interest in the speciality. The Faculty's mission is to advance the science and practice of pharmaceutical medicine by working to develop and maintain competence, ethics and integrity and the highest professional standards in the speciality for the benefit of the public. The Faculty seeks, through its activities, to bring about an improvement in the health of the public.

The duties of pharmaceutical physicians...

Physicians need additional training to be recognised as specialists. Appropriate training is, for example, that recognised by the Faculty of Pharmaceutical Medicine as suitable for the granting of its membership (MFPM). This should include training in medical ethics and international good clinical practices (GCPs); they should promote these principles by leadership and example and seek to raise standards of ethical conduct amongst their colleagues and fellow staff.

Pharmaceutical physicians should participate in regular training designed to ensure that their knowledge and practices parallel advances in their speciality. This should be extended to include special training in pharmacovigilance, local codes of practice and changes in the regulatory and ethical requirements relevant to their activities.

Regulatory Work

Pharmaceutical physicians play a key role in the judgement of suitability for use of any treatment by doctors and patients, and they must work to high ethical standards. They have an ethical responsibility to ensure that the proposed labelling of a medicinal product accurately reflects the clinical trials data. Decisions regarding proposed labelling and interactions with the regulatory agencies must be taken objectively, based on the available data and in terms of the wider public interest. Pharmaceutical physicians are accountable to their peers, to their managers and ultimately to society. Society needs new and better medicines, and regulators ultimately determine the labelling and restrictions that are most appropriate to their use, in regard to the balance between benefit and risk to the individual. In addition, pharmaceutical physicians working in a regulatory environment must continue to apply the same high standards as they evaluate the safety and utility of products already available to the public and prescribing clinicians.

Academic Work

Pharmaceutical physicians working in academic roles can have a major influence on perceptions of the importance and value of particular medicines. They, too, must put the consideration of the patient's best interests and any wider public benefit above any pressures for publication, grant application or other personal enhancement.



Publication

There should be openness and honesty in sharing the results of research. It is unethical to withhold the publication of any results of research on any pharmaceutical product whether the results are positive, negative or inconclusive.

Marketing Work

Pharmaceutical physicians may play many different roles in the marketing activities around pharmaceutical products. Similar ethical standards apply to them also. The well-being of any patient potentially receiving the medication is what matters most and must be given due prominence. The promotion of all medicines must be supervised by pharmaceutical physicians and be based on objective, ongoing assessment of all the available information, be in accordance with the labelling and not involve the use of undue pressures or inducements of any nature on healthcare workers to prescribe a product. Information provided to healthcare workers should permit objective clinical decision-making based on the merits of available products.

Programmes to assess and monitor the risk-benefit ratio of all medicines post-marketing must be devised and implemented. The results should be acted upon immediately and appropriately in the event of any safety signal.

Competing Interests

Pharmaceutical physicians, in whatever role they find themselves, be it regulatory, marketing, research, academia or otherwise, must declare all potential competing interests. They should take decisions that primarily protect the health and well-being of patients and research subjects, and also advance medical knowledge for the scientific and wider public benefit. Decisions should not be made to gain financial or other material benefits for themselves, their family or friends. Competing interests cover anything that might influence the making of balanced, unbiased judgements of importance to patients or research subjects. This includes potential competing interests in dealings with professional colleagues, scientific journals and the general public.

Research or Development Work

A registered medical practitioner with appropriate GCP training (in methodology, statistics and regulatory issues, for example) should be in overall direct control of research involving human subjects and be accountable (including being willing to submit to scrutiny) for decisions which impact on patient management and safety.

Guidelines for clinical trial methodology, ethics and good clinical practice...

Good Clinical Practice

All studies for which pharmaceutical physicians have responsibility must conform to GCP and any other relevant legislation and guidelines. The International Conference on Harmonisation (ICH) Guidelines for GCP, which make reference to the Declaration of Helsinki, have in recent years become the standard to be applied to clinical research practices in many countries throughout the world. The UK Faculty strongly endorses these recommended practices and standards. A pharmaceutical physician should be responsible for clinical research activities, although a non-medically qualified scientist may have executive responsibility for research and development within an institution or company. The pharmaceutical physician must ensure that the scientific approach is current and the clinical trial methodology is sound, the motivation is clear, the processes are unambiguous and that reasonable judgement on the safety and efficacy of any interventions proposed can be made on the basis of existing data. The research must be supported by sound study documentation. Furthermore, pharmaceutical physicians must have the skills and objectivity to interpret the results of clinical trials for which they are responsible and be prepared to speak out when there is a conflict between patient safety and commercial interests. Pharmaceutical physicians should not be placed nor place themselves under any financial or other obligations to individuals or groups, either within or outside their own organisation that might influence them in the performance of these duties.



Independent Review

Clinical study plans should be subject to either independent review or appraisal by senior management exercising clinical governance within a company or institution prior to starting any study, and prior to seeking written approval from an appropriately constituted research ethics committee. There should be openness about decisions and actions taken together with the justifications. All payment for service should be transparent, whether to investigators, their staff or external consultants. Payment to research subjects or others involved should be within the locally accepted range and should be declared to the research ethics committee. Prior to the clinical research being initiated, any potential conflicts of interest must be declared to the sponsor and the research ethics committee. Financial compensation of research subjects should be appropriate without constituting exploitation or inducement.

Study-Site Selection

The study sites chosen for a clinical trial should be appropriately equipped and selection based on objective criteria regarding the ability to recruit and manage patients in a clinical trial setting. The chief investigator and supporting staff at each site should be properly trained to care for the participating research subjects. The pharmaceutical physician in overall control has a duty to ensure that the local facilities are satisfactory, with a site-management system, and that GCPs are in operation throughout the study period.



Differing Standards of Care

Study designers may seek access to large and relatively under-treated patient groups wherever they can be found, either in developing or developed areas of the world. Nothing should be contemplated for study in a resource-poor group that could not ethically be done in a better-resourced country or region. Judgments of what is appropriate will vary according to social, ethical, economic and governmental factors, which are local and not necessarily international. The principles of beneficence and respect for human dignity must prevail everywhere. The proposed research should be relevant and of potential benefit to both the research participants and the host country. Prior to initiating the research, consideration should be given to the potential need to provide continuing care to the research subjects if justified by the clinical trial results.



The duties of pharmaceutical physicians to special and vulnerable patient groups...

Compensation

Arrangements and available details for product liability, indemnity and compensation in the event of anyone suffering damage should be made clear to potential research subjects, research ethics committees and all other interested parties.



Small Patient Groups

There are also special or small groups of patients who have been excluded from previous work, because they fall outside the accepted inclusion criteria approved for marketed products. The need to conduct clinical research in small patient groups should be clearly addressed within the master development plan and should take into consideration the views of the regulators, clinicians and needs of patients. Great caution should be exercised regarding the enrolment of such patients, and the independent ethical review will be challenging. Nevertheless, pharmaceutical physicians should give attention to the needs of such populations in drug development master plans. There is a great shortfall today in research knowledge derived from studies in the very young and the very old, for example, and this is not in the best interests of those patient groups.

Informed Consent

People volunteering to be research subjects, whether healthy volunteers or patient volunteers, are required to give written informed consent after receiving sufficient and properly witnessed explanations of the potential risks and benefits involved. Where this is not possible, for example in vulnerable groups such as the very young, the very old or the very sick, special permission must be obtained from the research ethics committee to ensure the safeguarding of the participants' best interests.

Ethnicity

The necessity of studying specific ethnic groups must be carefully weighed against the quality of the information that is likely to be generated and the use to which it will be put. It may be as unethical not to study selected ethnic groups and then to extrapolate results to them from a different ethnic group, as to study the minority group in the first place. Cross-sections from populations relevant to the intended users are ideal. Intrinsic factors such as genetic and metabolic variation as well as extrinsic factors like cultural and social values can complicate trial design, performance and interpretation of clinical study results, but should still be considered within the overall development plan.

Ability to Consent

There are patients who are not able to give free and informed consent to any intervention, for example some intensive care patients and infants. They can only be included with special precautions and should not be included in clinical studies except under special circumstances.



Orphan Indications

Where too few patients have a disease for a treatment to be fully and extensively investigated, evidence-based and carefully balanced judgements may not be possible. Development of new treatments within this category may fall under legislation for 'orphan' indications. As for 'mainstream' treatment indications, the pharmaceutical physician should ensure that all relevant and necessary information is made available to others who want, in their turn, to be able to give specific advice to patients or their families.

Sharing Findings

All studies should be performed to increase knowledge in some useful way, and there should be openness and honesty in the sharing of this knowledge with the wider world. Study findings need to be communicated, whatever the outcome, for the benefit of the community at large. The sponsor should have a clear policy regarding study publication which should be agreed with the clinical researcher prior to study initiation, and neither the sponsor nor the researcher should seek to prevent publication or the admission of trial results within the public domain. Communications on clinical studies must be a correct objective representation of all the findings, allowing others, in their turn, to give well-balanced risk-to-benefit advice to patients and their families. It is especially important that negative results or adverse safety data are communicated to regulators and clinicians in a timely manner where this information may affect prescribing practices and the protection of patients.