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Guiding Principles for Pharmaceutical Physicians from the Ethical Issues Committee of the Faculty of Pharmaceutical Medicine of the Royal Colleges of Physicians of the UK

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SUMMARY

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 wider society ahead of responsibilities to an individual employer while emphasising the importance of adherence to high standards of research, including dissemination of findings. These principles form the basis of a fuller report which offers more specific practical advice on possible ethical conflicts or dilemmas.

Keywords: Medical ethics; pharmaceutical medicine

EXECUTIVE SUMMARY

There are particular ethical issues which doctors practising within the discipline of pharmaceutical medicine may face. This paper sets out guiding principles with which to deal with those ethical issues which might face a pharmaceutical physician whether he or she is practising within a company, a contract research organisation, an academic department, a regulatory authority or elsewhere. It offers guidance and support to pharmaceutical physicians who are members of the UK Faculty as well as to others.

PROTECTION OF PATIENTS AND RESEARCH SUBJECTS

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.

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.

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.

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, London, UK (www.fpm.org.uk) as suitable for the granting of its membership (MFPM). This should include training in medical ethics and international good clinical practices (GCPs).

Pharmaceutical physicians should participate in regular training designed to ensure that their knowledge and practices parallel advances in their chosen 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.

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Publication

It is unethical to withhold the publication of any results of research on any pharmaceutical product whether the results are positive, negative or inconclusive.

Competing Interests

Pharmaceutical physicians, in whatever role they find themselves, be it regulatory, marketing, research, academia or otherwise, must declare all potential competing interests. 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.

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 interest above any pressures for publication, grant application or other personal enhancement.

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.

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. They 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.

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.

Programmes to assess and monitor the risk-benefit ratio 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.

CLINICAL TRIAL METHODOLOGY, ETHICS AND GCP

GCP

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.

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. 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. 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 undertreated 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. Judgements 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.

SPECIAL AND VULNERABLE PATIENT GROUPS

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.

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.

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.

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.

Sharing Findings

All studies should be performed to increase knowledge in some useful way, and this knowledge must be shared 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 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.

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APPENDIX

The Ethical Issues Committee of the Faculty of Pharmaceutical Medicine, London UK comprised the following members at the time of writing this report:

Dr Roger Bickerstaffe (Chairman)
Global Vice President Communications, Solvay Pharmaceuticals, Belgium and past chairman of the European Forum on Good Clinical Practice, Brussels

Dr Peter Brock
Medical Director, European Vice-President, Medical Affairs, Wyeth Lederle and Member of Association of British Pharmaceutical Industries Medical Committee

Prof. Jean-Marc Husson
Consultant Pharmaceutical Physician and Director of the European Diploma in Pharmaceutical Medicine. Past President of the International Federation of Associations of Pharmaceutical Physicians and past Medical Director, Roussel-Uclaf, Paris

Dr Ian Rubin
Chief Executive Officer, Matrix, past Medical Director, Fisons Pharmaceuticals and Chief Operations Officer and Medical Director, Phytopharm plc

Dr Keith Bragman
Consultant Pharmaceutical Physician. Past Director and Head of Global Development, UCB S.A, Brussels, Belgium

Dr Ken Paterson
Department of Clinical Pharmacology, Royal Infirmary, Glasgow and past Secretary to the Royal College of Physicians and Surgeons of Glasgow

Prof. Ann Sommerville
Visiting professor of Medical Ethics at Queen Mary College, London and Head of the British Medical Association's Ethics Department

