



TRIALS - from Nuremberg to Clinical

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The concept that a patient is expected to be a passive recipient of medical advice has changed dramatically over the past 25 years. Patients in today's society, as a rule, expect to be informed of the risks and benefits associated with their treatment in order that their consent can be given based on the information presented to them.

The Department of Health has issued a reference guide which states that "It is a general legal and ethical principle that valid consent must be obtained before starting treatment or physical investigation, or providing personal care, for a patient" (1) The Guide however, offers no real suggestions as to how much information should be offered in order to make the consent 'informed'.

This article seeks to provide an overview of the history and conduct of clinical trials, including the information which must be given to individual patients before they give informed consent to participate. This will allow the reader to compare the protection granted to the participants in clinical trials with that conferred on patients undergoing treatment.

All the drugs and many of the devices used on a daily basis throughout the health service will have undergone stringent examination in clinical trials to ensure that they are safe and to be used in patient care. Patients who consent to participate in clinical trials are protected by ethical and legal requirements contained in Directive 2001/20/EC of the European

Parliament. The provisions contained within the directive are aimed at protecting patients' rights to autonomy and self determination. Article 2(i) defines the procedure which should be adopted in obtaining informed consent and the fact that consent should be taken 'freely after being informed of its nature, significance, implications and risks....'(2)

The first formulation of a code for research on humans took place at Nuremberg in the wake of the appalling unethical experimentation, torture and murder perpetrated during the Second World War in the Nazi concentration camps. The subsequent trial of 23 physicians and scientists produced the Nuremberg Code (Directives for Human Experimentation) which begins with the now widely recognised

statement that 'the voluntary consent of the Human Subject is absolutely essential'(3). The Nuremberg code operated until the World Medical Association met at the International Conference on Harmonisation (ICH) in Finland to identify a set of ethical principles which would provide further guidance for medical researchers. This set of principles became known as The Declaration of Helsinki. The first declaration was adopted in June 1964 and has undergone revision several times in order to accommodate the advances in medical science and the ethical problems which these advances produce. The last revision took place when the 52nd World Medical Assembly (WMA) met in Edinburgh in October 2000.

Embedded within the Basic Principles of the

Declaration is the statement that 'the right of the research subject to safeguard his or her integrity must always be respected' (4). It also places a duty on the researcher to ensure that 'each potential subject must be adequately informed of the aims, methods, anticipated benefits and potential hazards of the study and the discomfort it may entail'(4). Known as the 'Ethical Principles for Medical Research involving Human Subjects' the declaration is the basis for the code of practice for clinical research. The guidelines influenced by the declaration are known as Good Clinical Practice (GCP). (5)

The regulation and standardisation of GCP throughout Europe is the remit of the EU Directive 2001/20/EC (2). At present the Directive is not legally enforceable, but in April 2003 it will be law in all the member states of the European Union. Clinical Trials must also maintain standards dictated by the Medical Research Council (MRC) and some trials with sites in the United States in addition to Europe come under the scrutiny of the Food and Drug Administration (FDA). If GCP guidelines are not adhered to inspectors from these agencies have the authority to close down a study if a serious breach has been detected.

All applications for the conduct of a clinical trial must be approved by the relevant ethics body. This includes the requirements for the obtaining of consent.

The Guidelines on obtaining informed consent (5) are comprehensive and are presented in order that the potential subject is fully aware of his rights and also his obligations during the conduct of the clinical trial. The list is comprehensive and identifies twenty aspects which should be communicated to the participant including one which states 'the alternative procedure(s) or course(s) of treatment that may be available to the subject, and their important potential benefits and risks' (5). The patient also can ask as many questions as he feels are necessary and should be given the information sheet, to read at home, several days prior to his consent being sought.

The main difference between clinical trial subjects and patients who require urgent medical interventions is obviously that the trial subject has the luxury of declining the offer to participate. Even some sources within the clinical trial field feel that "Fully informed consent can be needlessly cruel" in certain instances, suggesting that 'informed consent

should be viewed as another straightforward instance in which the clinical judgement of the doctor is paramount' (6)

However faced with the current increase in litigation and the demand for greater accountability the General Medical Council (GMC) has published guidance to doctors on obtaining consent.(7) The guidelines are both detailed and specific while advocating improved communications between doctor and patient.

In conclusion, having looked at the requirements expected of investigators in clinical trials and those of doctors within the healthcare system it would appear that they are, in essence, similar. The main difference is that the patient in clinical trials has the right to decline the offer to participate and his right to informed consent is unequivocal. The patient who is to undergo a procedure is perhaps at a disadvantage in that at present the information on which he might base his consent could be delivered by a doctor who still feels that he, as the doctor, knows what is best for his patient.

References:

- 1 Reference Guide to Consent for Examination or Treatment - Department of Health. Crown Copyright (2001)
- 2 Directive 2001/20/EC of the European Parliament. - Official Journal of the European Communities L121/34/01/05/2001
- 3 Directives for Human Experimentation. The Nuremberg Code (1947) <http://ohsr.od.nih.gov/nuremberg.php3>
- 4 Declaration of Helsinki. <http://www.wma.net>
- 5 ICH Harmonised Tripartite Guidelines for Good Clinical Practice (4.8-4.9). Brook Wood Medical Publications.
- 6 Tobias, JS; Sokhumi, RL. Fully Informed Consent Can be Needlessly Cruel. BMJ 307 (6913) 1199-1201
- 7 Seeking Patients' Consent: The GMC Considerations (November 1998) GMC. <http://www.gmc-uk.org/standards/consent.htm>

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